

FILE 'EMBASE, BIOSIS, SCISEARCH, MEDLINE, CAPLUS' ENTERED AT 13:53:21 ON  
10 MAY 2005

L2 5365 S APTAMER  
L3 22 S FIRST (W) BINDING (W) DOMAIN  
L4 39 S SECOND (W) BINDING (W) DOMAIN  
L5 0 S L2 AND L3 AND L4  
L6 0 S L2 AND L3  
L7 2 S L2 AND BIVALENT (W) BINDING (W) MOLECULE  
L8 1261398 S L2 AND AGONIST OR ANTAGONIST  
L9 39 S L2 AND AGONIST  
L10 304 S L2 AND ANTAGONIST  
L11 17 S L2 AND BIVALENT  
L12 2 DUP REM L7 (0 DUPLICATES REMOVED)  
L13 29 DUP REM L9 (10 DUPLICATES REMOVED)  
L14 9 DUP REM L11 (8 DUPLICATES REMOVED)

FILE 'STNGUIDE' ENTERED AT 13:58:16 ON 10 MAY 2005

FILE 'CAPLUS' ENTERED AT 13:59:47 ON 10 MAY 2005

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10 MAY 2005

FILE 'STNGUIDE' ENTERED AT 14:01:23 ON 10 MAY 2005

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=> s aptamer  
L2 5365 APTAMER

=> s first (w) binding (w) domain  
L3 22 FIRST (W) BINDING (W) DOMAIN

=> s second (w) binding (w) domain  
L4 39 SECOND (W) BINDING (W) DOMAIN

=> s l2 and l3 and l4  
L5 0 L2 AND L3 AND L4

=> s l2 and l3  
L6 0 L2 AND L3

=> s l2 and bivalent (w) binding (w) molecule  
L7 2 L2 AND BIVALENT (W) BINDING (W) MOLECULE

=> s l2 and agonist or antagonist  
L8 1261398 L2 AND AGONIST OR ANTAGONIST

=> s l2 and agonist  
L9 39 L2 AND AGONIST

=> s l2 and antagonist  
L10 304 L2 AND ANTAGONIST

=> s l2 and bivalent  
L11 17 L2 AND BIVALENT

=> dup rem 17  
PROCESSING COMPLETED FOR L7  
L12 2 DUP REM L7 (0 DUPLICATES REMOVED)

=> dup rem 19  
PROCESSING COMPLETED FOR L9  
L13 29 DUP REM L9 (10 DUPLICATES REMOVED)

=> dup rem 111  
PROCESSING COMPLETED FOR L11  
L14 9 DUP REM L11 (8 DUPLICATES REMOVED)

=> d l2 iall

L2 ANSWER 1 OF 5365 EMBASE COPYRIGHT 2005 ELSEVIER INC. ALL RIGHTS

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ACCESSION NUMBER: 2005170456 EMBASE  
TITLE: Allosteric **aptamers** and aptazymes as probes for screening approaches.  
AUTHOR: Famulok M.  
CORPORATE SOURCE: M. Famulok, Rheinische Friedrich-Wilhelms-Univ., Kekule Inst. Organ. Chem./Biochemie, Gerhard-Domagk-Strasse 1, Bonn 53121, Germany. m.famulok@uni-bonn.de  
SOURCE: Current Opinion in Molecular Therapeutics, (2005) Vol. 7, No. 2, pp. 137-143.  
Refs: 58  
ISSN: 1464-8431 CODEN: CUOTFO  
COUNTRY: United Kingdom  
DOCUMENT TYPE: Journal; General Review  
FILE SEGMENT: 029 Clinical Biochemistry  
LANGUAGE: English  
SUMMARY LANGUAGE: English  
ENTRY DATE: Entered STN: 20050428  
Last Updated on STN: 20050428  
ABSTRACT: Substantial effort is currently being devoted to engineering allosteric nucleic acids, **aptamers** and ribozymes for various applications in cellular and molecular biology, biotechnology and diagnostics. These molecular switches alter their different functional activities in response to specific binding molecules, including proteins, nucleic acids and small organic compounds. The interacting molecules trigger a response in the allosteric nucleic acid, which can be used for purposes such as real-time monitoring, high-throughput screening or gene expression control. .COPYRGT. The Thomson Corporation.

CONTROLLED TERM: Medical Descriptors:  
allosterism  
cytology  
molecular biology  
biotechnological procedures  
diagnostic procedure  
protein binding  
high throughput screening  
gene expression  
reverse transcription polymerase chain reaction  
ligand binding  
in vitro study  
in vivo study  
Human immunodeficiency virus 1  
enzyme activity  
protein phosphorylation  
mammal cell  
transcription regulation  
Neurospora crassa  
Saccharomyces cerevisiae  
Schistosoma mansoni  
Escherichia coli  
molecular probe  
nonhuman  
review  
Drug Descriptors:  
**\*aptamer**  
nucleic acid  
ribozyme  
organic compound  
adenosine triphosphate  
flavine mononucleotide  
green fluorescent protein

luciferase  
 Rev protein: EC, endogenous compound  
 self splicing ribosomal RNA  
 beta galactosidase: EC, endogenous compound  
 CAS REGISTRY NO.: (adenosine triphosphate) 15237-44-2, 56-65-5, 987-65-5;  
 (flavine mononucleotide) 130-40-5, 146-17-8; (luciferase)  
 61970-00-1, 9014-00-0; (Rev protein) 111804-97-8,  
 127004-89-1

=> FIL STNGUIDE

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	41.64	43.03

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FILE CONTAINS CURRENT INFORMATION.

LAST RELOADED: May 6, 2005 (20050506/UP).

=> d 1-2 112 iall

YOU HAVE REQUESTED DATA FROM FILE 'CAPLUS' - CONTINUE? (Y)/N:y

L12 ANSWER 1 OF 2 CAPLUS COPYRIGHT 2005 ACS on STN  
 ACCESSION NUMBER: 2004:70006 CAPLUS  
 DOCUMENT NUMBER: 140:123646  
 ENTRY DATE: Entered STN: 28 Jan 2004  
 TITLE: Method of screening for bivalent binding nucleic acid  
 ligands (**aptamers**) of 7 transmembrane G  
 protein-coupled receptors for therapeutic and  
 diagnostic use  
 INVENTOR(S): Gold, Larry  
 PATENT ASSIGNEE(S): Gilead Sciences, Inc., USA  
 SOURCE: U.S., 17 pp., Cont.-in-part of U.S. Ser. No. 956,699.  
 CODEN: USXXAM  
 DOCUMENT TYPE: Patent  
 LANGUAGE: English  
 INT. PATENT CLASSIF.:  
     MAIN: C12Q001-68  
     SECONDARY: C12P019-34  
 US PATENT CLASSIF.: 435006000; 435091200; 935077000; 935078000; 536023100;  
 536025400  
 CLASSIFICATION: 3-1 (Biochemical Genetics)  
 Section cross-reference(s): 2, 9, 63  
 FAMILY ACC. NUM. COUNT: 127  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 6682886	B1	20040127	US 1998-118525	19980717
US 5683867	A	19971104	US 1994-234997	19940428
US 6083696	A	20000704	US 1997-956699	19971023
WO 2000004184	A1	20000127	WO 1999-US14853	19990630
W:	AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM,			

TR, TT, UA, UG, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM  
 RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK,  
 ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG,  
 CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG  
 AU 9947287 A1 20000207 AU 1999-47287 19990630  
 EP 1100960 A1 20010523 EP 1999-930840 19990630  
 R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,  
 IE, FI  
 AU 773741 B2 20040603 AU 2001-18257 20010202  
 AU 773815 B2 20040610 AU 2001-29834 20010323  
 US 2004091931 A1 20040513 US 2003-729667 20031205  
 PRIORITY APPLN. INFO.: US 1994-234997 A1 19940428  
 US 1997-956699 A2 19971023  
 US 1990-536428 B2 19900611  
 AU 1991-82061 A0 19910610  
 US 1991-714131 A2 19910610  
 US 1993-117991 B2 19930908  
 US 1993-123935 B2 19930917  
 US 1994-199507 A2 19940222  
 US 1994-234797 A2 19940428  
 AU 1996-58839 A3 19960530  
 AU 1996-61611 A3 19960604  
 US 1998-118525 A 19980717  
 WO 1999-US14853 W 19990630

PATENT CLASSIFICATION CODES:

PATENT NO.	CLASS	PATENT FAMILY CLASSIFICATION CODES
US 6682886	ICM	C12Q001-68
	ICS	C12P019-34
	INCL	435006000; 435091200; 935077000; 935078000; 536023100; 536025400
US 6682886	NCL	435/006.000; 435/091.200; 536/023.100; 536/025.400
US 5683867	NCL	435/006.000; 435/091.200; 536/023.100; 536/025.400
	ECLA	C07H019/06E; C07H019/10E; C07H021/00C2; C07H021/00C4; C12N015/10C4; C12N015/11D; C12Q001/68A8+525/101; C12Q001/68A8; G01N033/532; G01N033/535; G01N033/68; G01N033/76
US 6083696	NCL	435/006.000; 435/091.200; 536/023.100; 536/024.300; 536/025.400
WO 2000004184	ECLA	C12Q001/68A8
US 2004091931	NCL	435/006.000; 435/007.100; 435/069.100; 435/320.100; 435/325.000; 530/350.000; 525/054.100; 530/395.000

ABSTRACT:

**Methods for identifying and preparing bivalent binding mols.** to 7 transmembrane domain containing G protein-coupled receptors, that can activate or inhibit 7 transmembrane G protein-coupled receptors, are described. SELEX (Systematic Evolution of Ligands by EXponential enrichment) method is used to screening high affinity nucleic acid ligands, also termed **aptamers.** It combines two or more binding domains to two or more different epitopes of the same 7 transmembrane G protein-coupled receptor. These SELEX-derived **bivalent binding mols.** comprise two or more binding domains which bind simultaneously to two or more epitopes of the same 7TM G protein-coupled receptor, thus has increased binding affinity to 7TM G protein-coupled receptor for their activation or inhibition. The method was exemplified by screening random RNA libraries for binding mols. to both ECL1 (extracellular loop 1) or ECL2 of neurokinin receptor NK1R using peptide affinity columns. The bivalent ligands, derived from two ECL1- and ECL1-binding RNA libraries by linking them through overlap-extension PCR reaction, can be enriched after cycles of SELEX process to generate double-stranded DNA templates for their future synthesis. These **bivalent binding mols.** may be useful as therapeutic and diagnostic agents.

SUPPL. TERM: drug screening bivalent **aptamer** 7TM G protein coupled receptor

INDEX TERM: Neurotensin receptors  
ROLE: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)  
(A, of human, screening for bivalent nuclear acid ligands binding to peptides of; method of screening for bivalent binding **aptamers** of 7 transmembrane GPCRs for therapeutic and diagnostic use)

INDEX TERM: Parathyroid hormone receptors

Secretin receptors  
ROLE: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)  
(A, of rat/opossum, screening for bivalent nuclear acid ligands binding to peptides of; method of screening for bivalent binding **aptamers** of 7 transmembrane GPCRs for therapeutic and diagnostic use)

INDEX TERM: Adenosine receptors  
ROLE: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)  
(A1, of rat or human or canine, screening for bivalent nuclear acid ligands binding to; method of screening for bivalent binding **aptamers** of 7 transmembrane GPCRs for therapeutic and diagnostic use)

INDEX TERM: Adenosine receptors  
ROLE: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)  
(A2B, of rat or human or sheep, screening for bivalent nuclear acid ligands binding to; method of screening for bivalent binding **aptamers** of 7 transmembrane GPCRs for therapeutic and diagnostic use)

INDEX TERM: Adenosine receptors  
ROLE: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)  
(A3, of human or sheep, screening for bivalent nuclear acid ligands binding to; method of screening for bivalent binding **aptamers** of 7 transmembrane GPCRs for therapeutic and diagnostic use)

INDEX TERM: Bradykinin receptors  
ROLE: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)  
(B2, of human/rat, screening for bivalent nuclear acid ligands binding to peptides of; method of screening for bivalent binding **aptamers** of 7 transmembrane GPCRs for therapeutic and diagnostic use)

INDEX TERM: Cholecystokinin receptors  
ROLE: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)  
(CCKA, of human/rat, screening for bivalent nuclear acid ligands binding to peptides of; method of screening for bivalent binding **aptamers** of 7 transmembrane GPCRs for therapeutic and diagnostic use)

INDEX TERM: Cholecystokinin receptors  
ROLE: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)  
(CCKB, of canine or human, screening for bivalent nuclear acid ligands binding to peptides of; method of screening for bivalent binding **aptamers** of 7 transmembrane GPCRs for therapeutic and diagnostic use)

INDEX TERM: Dopamine receptors  
ROLE: BUU (Biological use, unclassified); BIOL (Biological

study); USES (Uses)  
(D1, of rat or human or rhesus, screening for bivalent nuclear acid ligands binding to; method of screening for bivalent binding **aptamers** of 7 transmembrane GPCRs for therapeutic and diagnostic use)

INDEX TERM: Dopamine receptors  
ROLE: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)  
(D1A, of rat or human or rhesus, screening for bivalent nuclear acid ligands binding to; method of screening for bivalent binding **aptamers** of 7 transmembrane GPCRs for therapeutic and diagnostic use)

INDEX TERM: Dopamine receptors  
ROLE: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)  
(D2, of rat or human or mouse, screening for bivalent nuclear acid ligands binding to; method of screening for bivalent binding **aptamers** of 7 transmembrane GPCRs for therapeutic and diagnostic use)

INDEX TERM: Dopamine receptors  
ROLE: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)  
(D3, of rat or human, screening for bivalent nuclear acid ligands binding to; method of screening for bivalent binding **aptamers** of 7 transmembrane GPCRs for therapeutic and diagnostic use)

INDEX TERM: Dopamine receptors  
ROLE: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)  
(D4, of human, screening for bivalent nuclear acid ligands binding to; method of screening for bivalent binding **aptamers** of 7 transmembrane GPCRs for therapeutic and diagnostic use)

INDEX TERM: Dopamine receptors  
ROLE: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)  
(D5, of rat or human, screening for bivalent nuclear acid ligands binding to; method of screening for bivalent binding **aptamers** of 7 transmembrane GPCRs for therapeutic and diagnostic use)

INDEX TERM: 5-HT receptors  
ROLE: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)  
(GP2-7 or 5A or 5A(S12) or 5B, of mouse/human, screening for bivalent nuclear acid ligands binding to peptides of; method of screening for bivalent binding **aptamers** of 7 transmembrane GPCRs for therapeutic and diagnostic use)

INDEX TERM: Histamine receptors  
ROLE: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)  
(H1, of bovine, screening for bivalent nuclear acid ligands binding to; method of screening for bivalent binding **aptamers** of 7 transmembrane GPCRs for therapeutic and diagnostic use)

INDEX TERM: Histamine receptors  
ROLE: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)  
(H2, of rat or canine or human, screening for bivalent nuclear acid ligands binding to; method of screening for bivalent binding **aptamers** of 7 transmembrane GPCRs for therapeutic and diagnostic use)

INDEX TERM: Muscarinic receptors  
ROLE: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)  
(M1, of mouse or human, screening for bivalent nuclear acid ligands binding to; method of screening for bivalent binding **aptamers** of 7 transmembrane GPCRs for therapeutic and diagnostic use)

INDEX TERM: Muscarinic receptors  
ROLE: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)  
(M2, of human, screening for bivalent nuclear acid ligands binding to; method of screening for bivalent binding **aptamers** of 7 transmembrane GPCRs for therapeutic and diagnostic use)

INDEX TERM: Muscarinic receptors  
ROLE: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)  
(M3, of human, screening for bivalent nuclear acid ligands binding to; method of screening for bivalent binding **aptamers** of 7 transmembrane GPCRs for therapeutic and diagnostic use)

INDEX TERM: Muscarinic receptors  
ROLE: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)  
(M4, of human or chicken, screening for bivalent nuclear acid ligands binding to; method of screening for bivalent binding **aptamers** of 7 transmembrane GPCRs for therapeutic and diagnostic use)

INDEX TERM: Muscarinic receptors  
ROLE: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)  
(M5, of human/rat, screening for bivalent nuclear acid ligands binding to; method of screening for bivalent binding **aptamers** of 7 transmembrane GPCRs for therapeutic and diagnostic use)

INDEX TERM: Oligonucleotides  
ROLE: BSU (Biological study, unclassified); PUR (Purification or recovery); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)  
(RNA **aptamers**, binding to G protein coupled-receptor epitopes; method of screening for bivalent binding **aptamers** of 7 transmembrane GPCRs for therapeutic and diagnostic use)

INDEX TERM: Genetic methods  
(SELEX; method of screening for bivalent binding **aptamers** of 7 transmembrane GPCRs for therapeutic and diagnostic use)

INDEX TERM: Somatostatin receptors  
ROLE: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)  
(SSTR1, of rat/human, screening for bivalent nuclear acid ligands binding to peptides of; method of screening for bivalent binding **aptamers** of 7 transmembrane GPCRs for therapeutic and diagnostic use)

INDEX TERM: Somatostatin receptors  
ROLE: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)  
(SSTR2, of mouse, screening for bivalent nuclear acid ligands binding to peptides of; method of screening for bivalent binding **aptamers** of 7 transmembrane GPCRs for therapeutic and diagnostic use)

INDEX TERM: Somatostatin receptors

INDEX TERM: **Somatostatin receptors**  
ROLE: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)  
(SSTR3, of rat/human/mouse, screening for bivalent nuclear acid ligands binding to peptides of; method of screening for bivalent binding **aptamers** of 7 transmembrane GPCRs for therapeutic and diagnostic use)

INDEX TERM: **Somatostatin receptors**  
ROLE: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)  
(SSTR4, of human/mouse, screening for bivalent nuclear acid ligands binding to peptides of; method of screening for bivalent binding **aptamers** of 7 transmembrane GPCRs for therapeutic and diagnostic use)

INDEX TERM: **Somatostatin receptors**  
ROLE: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)  
(SSTR5, of human/mouse, screening for bivalent nuclear acid ligands binding to peptides of; method of screening for bivalent binding **aptamers** of 7 transmembrane GPCRs for therapeutic and diagnostic use)

INDEX TERM: **Polysiloxanes, biological studies**  
ROLE: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)  
(amino, **aptamers** linked by; method of screening for bivalent binding **aptamers** of 7 transmembrane GPCRs for therapeutic and diagnostic use)

INDEX TERM: **Angiotensin receptors**  
ROLE: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)  
(angiotensin II, of human/rat/mouse, screening for bivalent nuclear acid ligands binding to peptides of; method of screening for bivalent binding **aptamers** of 7 transmembrane GPCRs for therapeutic and diagnostic use)

INDEX TERM: **Liposomes**  
(**aptamers** linked by; method of screening for bivalent binding **aptamers** of 7 transmembrane GPCRs for therapeutic and diagnostic use)

INDEX TERM: **Hydrocarbons, biological studies**  
**Monosaccharides**  
**Oligosaccharides, biological studies**  
**Peptides, biological studies**  
**Polynucleotides**  
**Polyoxyalkylenes, biological studies**  
**Proteins**  
ROLE: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)  
(**aptamers** linked by; method of screening for bivalent binding **aptamers** of 7 transmembrane GPCRs for therapeutic and diagnostic use)

INDEX TERM: **Polysiloxanes, biological studies**  
ROLE: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)  
(hydroxy, **aptamers** linked by; method of screening for bivalent binding **aptamers** of 7 transmembrane GPCRs for therapeutic and diagnostic use)

INDEX TERM: **DNA**  
ROLE: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)  
(linker, for generation of bivalent RNA ligands to G protein-coupled receptors epitopes; method of screening for bivalent binding **aptamers** of 7

INDEX TERM: transmembrane GPCRs for therapeutic and diagnostic use)  
Canis familiaris  
Human  
Mus  
Rattus  
(method of screening for bivalent binding  
**aptamers** of 7 transmembrane GPCRs for therapeutic  
and diagnostic use)

INDEX TERM: G protein-coupled receptors  
ROLE: BSU (Biological study, unclassified); BIOL (Biological  
study)  
(method of screening for bivalent binding  
**aptamers** of 7 transmembrane GPCRs for therapeutic  
and diagnostic use)

INDEX TERM: Epitopes  
(of G protein-coupled receptors; method of screening for  
bivalent binding **aptamers** of 7 transmembrane  
GPCRs for therapeutic and diagnostic use)

INDEX TERM: Thyrotropin receptors  
ROLE: BUU (Biological use, unclassified); BIOL (Biological  
study); USES (Uses)  
(of canine/rat or human, screening for bivalent nuclear  
acid ligands binding to peptides of; method of screening  
for bivalent binding **aptamers** of 7  
transmembrane GPCRs for therapeutic and diagnostic use)

INDEX TERM: Gonadotropin-releasing hormone receptor  
VIP receptors  
ROLE: BUU (Biological use, unclassified); BIOL (Biological  
study); USES (Uses)  
(of human, screening for bivalent nuclear acid ligands  
binding to peptides of; method of screening for bivalent  
binding **aptamers** of 7 transmembrane GPCRs for  
therapeutic and diagnostic use)

INDEX TERM: Gonadotropin receptors  
ROLE: BUU (Biological use, unclassified); BIOL (Biological  
study); USES (Uses)  
(of human/rat/mouse, screening for bivalent nuclear acid  
ligands binding to peptides of; method of screening for  
bivalent binding **aptamers** of 7 transmembrane  
GPCRs for therapeutic and diagnostic use)

INDEX TERM: Calcitonin receptors  
ROLE: BUU (Biological use, unclassified); BIOL (Biological  
study); USES (Uses)  
(of human/rat/pig, screening for bivalent nuclear acid  
ligands binding to peptides of; method of screening for  
bivalent binding **aptamers** of 7 transmembrane  
GPCRs for therapeutic and diagnostic use)

INDEX TERM: Corticotropin releasing factor receptors  
Glucagon receptors  
Growth hormone-releasing hormone receptors  
Neuropeptide Y receptors  
ROLE: BUU (Biological use, unclassified); BIOL (Biological  
study); USES (Uses)  
(of rat, screening for bivalent nuclear acid ligands  
binding to peptides of; method of screening for bivalent  
binding **aptamers** of 7 transmembrane GPCRs for  
therapeutic and diagnostic use)

INDEX TERM: Muscarinic receptors  
ROLE: BUU (Biological use, unclassified); BIOL (Biological  
study); USES (Uses)  
(of swine or Drosophila, screening for bivalent nuclear  
acid ligands binding to; method of screening for bivalent

INDEX TERM: binding **aptamers** of 7 transmembrane GPCRs for therapeutic and diagnostic use)

INDEX TERM: Affinity chromatography (screening for bivalent ligand to G protein-coupled receptors epitopes; method of screening for bivalent binding **aptamers** of 7 transmembrane GPCRs for therapeutic and diagnostic use)

INDEX TERM: Polysiloxanes, biological studies

ROLE: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)

(thio or carboxy-functionalized, **aptamers** linked by; method of screening for bivalent binding **aptamers** of 7 transmembrane GPCRs for therapeutic and diagnostic use)

INDEX TERM: PCR (polymerase chain reaction)

(to link G protein coupled receptor epitope ECL1- or ECL2-binding RNA mols.; method of screening for bivalent binding **aptamers** of 7 transmembrane GPCRs for therapeutic and diagnostic use)

INDEX TERM: 5-HT receptors

ROLE: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)

(type 5-HT1, 1C, of mouse/human, screening for bivalent nuclear acid ligands binding to peptides of; method of screening for bivalent binding **aptamers** of 7 transmembrane GPCRs for therapeutic and diagnostic use)

INDEX TERM: 5-HT receptors

ROLE: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)

(type 5-HT1, of rat, screening for bivalent nuclear acid ligands binding to peptides of; method of screening for bivalent binding **aptamers** of 7 transmembrane GPCRs for therapeutic and diagnostic use)

INDEX TERM: 5-HT receptors

ROLE: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)

(type 5-HT1A, of rat/human, screening for bivalent nuclear acid ligands binding to peptides of; method of screening for bivalent binding **aptamers** of 7 transmembrane GPCRs for therapeutic and diagnostic use)

INDEX TERM: 5-HT receptors

ROLE: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)

(type 5-HT1B, of rat/human/mouse, screening for bivalent nuclear acid ligands binding to peptides of; method of screening for bivalent binding **aptamers** of 7 transmembrane GPCRs for therapeutic and diagnostic use)

INDEX TERM: 5-HT receptors

ROLE: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)

(type 5-HT1D, of canine/human, screening for bivalent nuclear acid ligands binding to peptides of; method of screening for bivalent binding **aptamers** of 7 transmembrane GPCRs for therapeutic and diagnostic use)

INDEX TERM: 5-HT receptors

ROLE: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)

(type 5-HT1E, of rat, screening for bivalent nuclear acid ligands binding to peptides of; method of screening for bivalent binding **aptamers** of 7 transmembrane GPCRs for therapeutic and diagnostic use)

INDEX TERM: 5-HT receptors

INDEX TERM: 5-HT receptors  
ROLE: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)  
(type 5-HT2, of rat, screening for bivalent nuclear acid ligands binding to peptides of; method of screening for bivalent binding **aptamers** of 7 transmembrane GPCRs for therapeutic and diagnostic use)

INDEX TERM: 5-HT receptors  
ROLE: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)  
(type 5-HT2B, of human, screening for bivalent nuclear acid ligands binding to peptides of; method of screening for bivalent binding **aptamers** of 7 transmembrane GPCRs for therapeutic and diagnostic use)

INDEX TERM: 5-HT receptors  
ROLE: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)  
(type 5-HT3, of mouse, screening for bivalent nuclear acid ligands binding to peptides of; method of screening for bivalent binding **aptamers** of 7 transmembrane GPCRs for therapeutic and diagnostic use)

INDEX TERM: 5-HT receptors  
ROLE: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)  
(type 5-HT7, of rat, screening for bivalent nuclear acid ligands binding to peptides of; method of screening for bivalent binding **aptamers** of 7 transmembrane GPCRs for therapeutic and diagnostic use)

INDEX TERM: Endothelin receptors  
ROLE: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)  
(type ETB, of human, screening for bivalent nuclear acid ligands binding to peptides of; method of screening for bivalent binding **aptamers** of 7 transmembrane GPCRs for therapeutic and diagnostic use)

INDEX TERM: Tachykinin receptors  
ROLE: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)  
(type NK1, of human/mouse/rat, screening for bivalent nuclear acid ligands binding to peptides of; method of screening for bivalent binding **aptamers** of 7 transmembrane GPCRs for therapeutic and diagnostic use)

INDEX TERM: Opioid receptors  
ROLE: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)  
( $\kappa$ -opioid, of human/rat/mouse, screening for bivalent nuclear acid ligands binding to; method of screening for bivalent binding **aptamers** of 7 transmembrane GPCRs for therapeutic and diagnostic use)

INDEX TERM: Adrenoceptors  
ROLE: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)  
( $\alpha_1$ , of hamster or bovine, screening for bivalent nuclear acid ligands binding to; method of screening for bivalent binding **aptamers** of 7 transmembrane GPCRs for therapeutic and diagnostic use)

INDEX TERM: Adrenoceptors  
ROLE: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)  
( $\alpha_1D$ , of rat, screening for bivalent nuclear acid ligands binding to; method of screening for bivalent binding **aptamers** of 7 transmembrane GPCRs for therapeutic and diagnostic use)

INDEX TERM: Adrenoceptors  
ROLE: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)  
( $\alpha$ 2, of human or mouse or fish, screening for bivalent nuclear acid ligands binding to; method of screening for bivalent binding **aptamers** of 7 transmembrane GPCRs for therapeutic and diagnostic use)

INDEX TERM: Adrenoceptors  
ROLE: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)  
( $\alpha$ 2, of human or rat, screening for bivalent nuclear acid ligands binding to; method of screening for bivalent binding **aptamers** of 7 transmembrane GPCRs for therapeutic and diagnostic use)

INDEX TERM: Adrenoceptors  
ROLE: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)  
( $\alpha$ 2A, of human or porcine or rat, screening for bivalent nuclear acid ligands binding to; method of screening for bivalent binding **aptamers** of 7 transmembrane GPCRs for therapeutic and diagnostic use)

INDEX TERM: Adrenoceptors  
ROLE: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)  
( $\alpha$ 2B, of human or rat, screening for bivalent nuclear acid ligands binding to; method of screening for bivalent binding **aptamers** of 7 transmembrane GPCRs for therapeutic and diagnostic use)

INDEX TERM: Adrenoceptors  
ROLE: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)  
( $\alpha$ 2C, of mouse or rat, screening for bivalent nuclear acid ligands binding to; method of screening for bivalent binding **aptamers** of 7 transmembrane GPCRs for therapeutic and diagnostic use)

INDEX TERM: Adrenoceptors  
ROLE: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)  
( $\beta$ 1, of rat or human or mouse, screening for bivalent nuclear acid ligands binding to; method of screening for bivalent binding **aptamers** of 7 transmembrane GPCRs for therapeutic and diagnostic use)

INDEX TERM: Adrenoceptors  
ROLE: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)  
( $\beta$ 2, of rat or human or mouse, screening for bivalent nuclear acid ligands binding to; method of screening for bivalent binding **aptamers** of 7 transmembrane GPCRs for therapeutic and diagnostic use)

INDEX TERM: Adrenoceptors  
ROLE: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)  
( $\beta$ 3, of rat or human or bovine, screening for bivalent nuclear acid ligands binding to; method of screening for bivalent binding **aptamers** of 7 transmembrane GPCRs for therapeutic and diagnostic use)

INDEX TERM: Opioid receptors  
ROLE: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)  
( $\delta$ -opioid, of human/mouse, screening for bivalent nuclear acid ligands binding to; method of screening for bivalent binding **aptamers** of 7 transmembrane

INDEX TERM: GPCRs for therapeutic and diagnostic use)  
Opioid receptors  
ROLE: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)  
( $\mu$ -opioid, of human/rat, screening for bivalent nuclear acid ligands binding to; method of screening for bivalent binding **aptamers** of 7 transmembrane GPCRs for therapeutic and diagnostic use)

INDEX TERM: 9002-89-5, Ethenol, homopolymer 9003-01-4, 2-Propenoic acid homopolymer 9004-53-9, Dextrin 12619-70-4, Cyclodextrin 25322-68-3, Poly(oxy-1,2-ethanediyl),  $\alpha$ -hydro- $\omega$ -hydroxy- 25322-69-4, Poly[oxy(methyl-1,2-ethanediyl)],  $\alpha$ -hydro- $\omega$ -hydroxy-  
ROLE: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)  
(**aptamers** linked by; method of screening for bivalent binding **aptamers** of 7 transmembrane GPCRs for therapeutic and diagnostic use)

INDEX TERM: 268720-50-9P, RNA (synthetic)  
ROLE: BPN (Biosynthetic preparation); BSU (Biological study, unclassified); PUR (Purification or recovery); BIOL (Biological study); PREP (Preparation)  
(as ligands to G protein coupled-receptor; method of screening for bivalent binding **aptamers** of 7 transmembrane GPCRs for therapeutic and diagnostic use)

INDEX TERM: 255916-21-3, L-Phenylalanine, L-histidyl-L-asparaginyl-L- $\alpha$ -glutamyl-L-tryptophyl-L-tyrosyl-L-tyrosylglycyl-L-leucyl-L-phenylalanyl-L-tyrosyl-L-cysteinyl-L-lysyl-  
ROLE: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)  
(neurokinin receptor 1 extracellular loop 1; method of screening for bivalent binding **aptamers** of 7 transmembrane GPCRs for therapeutic and diagnostic use)

INDEX TERM: 255916-22-4, L-Valine, L-threonyl-L-threonyl-L- $\alpha$ -glutamyl-L-threonyl-L-methionyl-L-prolyl-L-seryl-L-arginyl-L-valyl-L-valyl-L-cysteinyl-L-methionyl-L-isoleucyl-L- $\alpha$ -glutamyl-L-tryptophyl-L-prolyl-L- $\alpha$ -glutamyl-L-histidyl-L-prolyl-L-asparaginyl-L-lysyl-L-isoleucyl-L-tyrosyl-L- $\alpha$ -glutamyl-L-lysyl-  
ROLE: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)  
(neurokinin receptor 1 extracellular loop 2; method of screening for bivalent binding **aptamers** of 7 transmembrane GPCRs for therapeutic and diagnostic use)

REFERENCE COUNT: 29 THERE ARE 29 CITED REFERENCES AVAILABLE FOR THIS RECORD.

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ACCESSION NUMBER: 2000:68592 CAPLUS  
 DOCUMENT NUMBER: 132:105019  
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 TITLE: Synthesis and identification of bivalent binding RNA molecules to G protein-coupled receptors  
 INVENTOR(S): Gold, Larry  
 PATENT ASSIGNEE(S): Nexstar Pharmaceuticals, Inc., USA  
 SOURCE: PCT Int. Appl., 49 pp.  
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W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
US 6682886	B1	20040127	US 1998-118525	19980717
AU 9947287	A1	20000207	AU 1999-47287	19990630
EP 1100960	A1	20010523	EP 1999-930840	19990630
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
AU 773741	B2	20040603	AU 2001-18257	20010202
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		US 1998-118525	A 19980717	
		AU 1991-82061	A0 19910610	
		US 1994-234997	A1 19940428	
		AU 1996-58839	A3 19960530	
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		US 1997-956699	A2 19971023	
		WO 1999-US14853	W 19990630	

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PATENT NO.	CLASS	PATENT FAMILY CLASSIFICATION CODES
WO 2000004184	ICM	C12Q001-68
	ICS	C12P019-34
WO 2000004184	ECLA	C12Q001/68A8
US 6682886	NCL	435/006.000; 435/091.200; 536/023.100; 536/025.400

## ABSTRACT:

Methods for identifying and preparing **bivalent binding**

\*\*\*mols.\*\*\* to 7 transmembrane domain containing G protein-coupled receptors are described. The methods are based on the SELEX method (Systematic Evolution of Ligands by EXponential enrichment) for generating high affinity nucleic acid ligands, termed **aptamers**. It combines two or more binding domains to two or more different epitopes of the same 7 transmembrane G protein-coupled receptor. The method was exemplified by screening in the random RNA library for binding mols. to either ECL1 (extracellular loop 1) or ECL2 of neurokinin receptor NK1R using peptide affinity columns. The bivalent ligands, derived from two ECL1- and ECL1-binding RNA libraries by linking them through overlap-extension PCR reaction, can be enriched after cycles of SELEX process to generate double-stranded DNA templates for their future synthesis. These \*\*\*bivalent\*\*\* **binding mols.** may be useful as therapeutic and diagnostic agents.

SUPPL. TERM: biosynthesis screening **bivalent binding**  
 mol G protein coupled receptor; **aptamers**  
 bivalent substance P receptor NK1R SELEX

INDEX TERM: 5-HT receptors  
 ROLE: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)  
 (5-HT1, 1C, of mouse/human, screening for bivalent nuclear acid ligands binding to peptides of; synthesis and identification of bivalent binding RNA mols. to G protein-coupled receptors)

INDEX TERM: 5-HT receptors  
 ROLE: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)  
 (5-HT1, of rat, screening for bivalent nuclear acid ligands binding to peptides of; synthesis and identification of bivalent binding RNA mols. to G protein-coupled receptors)

INDEX TERM: 5-HT receptors  
 ROLE: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)  
 (5-HT1A, of rat/human, screening for bivalent nuclear acid ligands binding to peptides of; synthesis and identification of bivalent binding RNA mols. to G protein-coupled receptors)

INDEX TERM: 5-HT receptors  
 ROLE: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)  
 (5-HT1B, of rat/human/mouse, screening for bivalent nuclear acid ligands binding to peptides of; synthesis and identification of bivalent binding RNA mols. to G protein-coupled receptors)

INDEX TERM: 5-HT receptors  
 ROLE: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)  
 (5-HT1D, of canine/human, screening for bivalent nuclear acid ligands binding to peptides of; synthesis and identification of bivalent binding RNA mols. to G protein-coupled receptors)

INDEX TERM: 5-HT receptors

INDEX TERM: 5-HT receptors  
ROLE: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)  
(5-HT1E, of rat, screening for bivalent nuclear acid ligands binding to peptides of; synthesis and identification of bivalent binding RNA mols. to G protein-coupled receptors)

INDEX TERM: 5-HT receptors  
ROLE: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)  
(5-HT2, of rat, screening for bivalent nuclear acid ligands binding to peptides of; synthesis and identification of bivalent binding RNA mols. to G protein-coupled receptors)

INDEX TERM: 5-HT receptors  
ROLE: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)  
(5-HT2B, of human, screening for bivalent nuclear acid ligands binding to peptides of; synthesis and identification of bivalent binding RNA mols. to G protein-coupled receptors)

INDEX TERM: 5-HT receptors  
ROLE: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)  
(5-HT3, of mouse, screening for bivalent nuclear acid ligands binding to peptides of; synthesis and identification of bivalent binding RNA mols. to G protein-coupled receptors)

INDEX TERM: 5-HT receptors  
ROLE: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)  
(5-HT7, of rat, screening for bivalent nuclear acid ligands binding to peptides of; synthesis and identification of bivalent binding RNA mols. to G protein-coupled receptors)

INDEX TERM: Neurotensin receptors  
ROLE: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)  
(A, of human, screening for bivalent nuclear acid ligands binding to peptides of; synthesis and identification of bivalent binding RNA mols. to G protein-coupled receptors)

INDEX TERM: Parathyroid hormone receptors  
Secretin receptors  
ROLE: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)  
(A, of rat/opossum, screening for bivalent nuclear acid ligands binding to peptides of; synthesis and identification of bivalent binding RNA mols. to G protein-coupled receptors)

INDEX TERM: Adenosine receptors  
ROLE: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)  
(A1, of rat or human or canine, screening for bivalent nuclear acid ligands binding to; synthesis and identification of bivalent binding RNA mols. to G protein-coupled receptors)

INDEX TERM: Adenosine receptors  
ROLE: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)  
(A2B, of rat or human or sheep, screening for bivalent nuclear acid ligands binding to; synthesis and identification of bivalent binding RNA mols. to G

INDEX TERM: protein-coupled receptors)  
Adenosine receptors  
ROLE: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)  
(A3, of human or sheep, screening for bivalent nuclear acid ligands binding to; synthesis and identification of bivalent binding RNA mols. to G protein-coupled receptors)  
INDEX TERM: Bradykinin receptors  
ROLE: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)  
(B2, of human/rat, screening for bivalent nuclear acid ligands binding to peptides of; synthesis and identification of bivalent binding RNA mols. to G protein-coupled receptors)  
INDEX TERM: Dopamine receptors  
ROLE: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)  
(D1, of rat or human or rhesus, screening for bivalent nuclear acid ligands binding to; synthesis and identification of bivalent binding RNA mols. to G protein-coupled receptors)  
INDEX TERM: Dopamine receptors  
ROLE: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)  
(D2, of rat or human or mouse, screening for bivalent nuclear acid ligands binding to; synthesis and identification of bivalent binding RNA mols. to G protein-coupled receptors)  
INDEX TERM: Dopamine receptors  
ROLE: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)  
(D3, of rat or human, screening for bivalent nuclear acid ligands binding to; synthesis and identification of bivalent binding RNA mols. to G protein-coupled receptors)  
INDEX TERM: Dopamine receptors  
ROLE: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)  
(D4, of human, screening for bivalent nuclear acid ligands binding to; synthesis and identification of bivalent binding RNA mols. to G protein-coupled receptors)  
INDEX TERM: Dopamine receptors  
ROLE: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)  
(D5, of rat or human, screening for bivalent nuclear acid ligands binding to; synthesis and identification of bivalent binding RNA mols. to G protein-coupled receptors)  
INDEX TERM: Endothelin receptors  
ROLE: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)  
(ETB, of human, screening for bivalent nuclear acid ligands binding to peptides of; synthesis and identification of bivalent binding RNA mols. to G protein-coupled receptors)  
INDEX TERM: 5-HT receptors  
ROLE: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)  
(GP2-7 or 5A or 5A(S12) or 5B, of mouse/human, screening for bivalent nuclear acid ligands binding to peptides of;

INDEX TERM: synthesis and identification of bivalent binding RNA mols. to G protein-coupled receptors)

Histamine receptors

ROLE: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)

(H1, of bovine, screening for bivalent nuclear acid ligands binding to; synthesis and identification of bivalent binding RNA mols. to G protein-coupled receptors)

INDEX TERM: Histamine receptors

ROLE: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)

(H2, of rat or canine or human, screening for bivalent nuclear acid ligands binding to; synthesis and identification of bivalent binding RNA mols. to G protein-coupled receptors)

INDEX TERM: Muscarinic receptors

ROLE: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)

(M1, of mouse or human, screening for bivalent nuclear acid ligands binding to; synthesis and identification of bivalent binding RNA mols. to G protein-coupled receptors)

INDEX TERM: Muscarinic receptors

ROLE: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)

(M2, of human, screening for bivalent nuclear acid ligands binding to; synthesis and identification of bivalent binding RNA mols. to G protein-coupled receptors)

INDEX TERM: Muscarinic receptors

ROLE: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)

(M3, of human, screening for bivalent nuclear acid ligands binding to; synthesis and identification of bivalent binding RNA mols. to G protein-coupled receptors)

INDEX TERM: Muscarinic receptors

ROLE: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)

(M4, of human or chicken, screening for bivalent nuclear acid ligands binding to; synthesis and identification of bivalent binding RNA mols. to G protein-coupled receptors)

INDEX TERM: Muscarinic receptors

ROLE: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)

(M5, of human/rat, screening for bivalent nuclear acid ligands binding to; synthesis and identification of bivalent binding RNA mols. to G protein-coupled receptors)

INDEX TERM: Tachykinin receptors

ROLE: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)

(NK1, of human/mouse/rat, screening for bivalent nuclear acid ligands binding to peptides of; synthesis and identification of bivalent binding RNA mols. to G protein-coupled receptors)

INDEX TERM: Oligonucleotides

ROLE: BAC (Biological activity or effector, except adverse); BPN (Biosynthetic preparation); BSU (Biological study, unclassified); PUR (Purification or recovery); BIOL

INDEX TERM: (Biological study); PREP (Preparation)  
(RNA **aptamers**, binding to G protein  
coupled-receptor epitopes; synthesis and identification  
of bivalent binding RNA mols. to G protein-coupled  
receptors)

INDEX TERM: Genetic methods  
(SELEX; synthesis and identification of bivalent binding  
RNA mols. to G protein-coupled receptors)

INDEX TERM: Somatostatin receptors  
ROLE: BUU (Biological use, unclassified); BIOL (Biological  
study); USES (Uses)  
(SSTR1, of rat/human, screening for bivalent nuclear acid  
ligands binding to peptides of; synthesis and  
identification of bivalent binding RNA mols. to G  
protein-coupled receptors)

INDEX TERM: Somatostatin receptors  
ROLE: BUU (Biological use, unclassified); BIOL (Biological  
study); USES (Uses)  
(SSTR2, of mouse, screening for bivalent nuclear acid  
ligands binding to peptides of; synthesis and  
identification of bivalent binding RNA mols. to G  
protein-coupled receptors)

INDEX TERM: Somatostatin receptors  
ROLE: BUU (Biological use, unclassified); BIOL (Biological  
study); USES (Uses)  
(SSTR3, of rat/human/mouse, screening for bivalent  
nuclear acid ligands binding to peptides of; synthesis  
and identification of bivalent binding RNA mols. to G  
protein-coupled receptors)

INDEX TERM: Somatostatin receptors  
ROLE: BUU (Biological use, unclassified); BIOL (Biological  
study); USES (Uses)  
(SSTR4, of human/mouse, screening for bivalent nuclear  
acid ligands binding to peptides of; synthesis and  
identification of bivalent binding RNA mols. to G  
protein-coupled receptors)

INDEX TERM: Somatostatin receptors  
ROLE: BUU (Biological use, unclassified); BIOL (Biological  
study); USES (Uses)  
(SSTR5, of human/mouse, screening for bivalent nuclear  
acid ligands binding to peptides of; synthesis and  
identification of bivalent binding RNA mols. to G  
protein-coupled receptors)

INDEX TERM: Polysiloxanes, biological studies  
ROLE: BUU (Biological use, unclassified); BIOL (Biological  
study); USES (Uses)  
(amino, **aptamers** linked by; synthesis and  
identification of bivalent binding RNA mols. to G  
protein-coupled receptors)

INDEX TERM: Angiotensin receptors  
ROLE: BUU (Biological use, unclassified); BIOL (Biological  
study); USES (Uses)  
(angiotensin II, of human/rat/mouse, screening for  
bivalent nuclear acid ligands binding to peptides of;  
synthesis and identification of bivalent binding RNA  
mols. to G protein-coupled receptors)

INDEX TERM: Liposomes  
(**aptamers** linked by; synthesis and  
identification of bivalent binding RNA mols. to G  
protein-coupled receptors)

INDEX TERM: Hydrocarbons, biological studies  
Monosaccharides

INDEX TERM: Oligosaccharides, biological studies  
Peptides, biological studies  
Polynucleotides  
Polyoxyalkylenes, biological studies  
Proteins, general, biological studies  
ROLE: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)  
    (aptamers linked by; synthesis and identification of bivalent binding RNA mols. to G protein-coupled receptors)

INDEX TERM: Cholecystokinin receptors  
ROLE: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)  
    (cholecystokinin A, of human/rat, screening for bivalent nuclear acid ligands binding to peptides of; synthesis and identification of bivalent binding RNA mols. to G protein-coupled receptors)

INDEX TERM: Cholecystokinin receptors  
ROLE: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)  
    (cholecystokinin B, of canine or human, screening for bivalent nuclear acid ligands binding to peptides of; synthesis and identification of bivalent binding RNA mols. to G protein-coupled receptors)

INDEX TERM: Polysiloxanes, biological studies  
ROLE: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)  
    (hydroxy, aptamers linked by; synthesis and identification of bivalent binding RNA mols. to G protein-coupled receptors)

INDEX TERM: DNA  
ROLE: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)  
    (linker, for generation of bivalent RNA ligands to G protein-coupled receptors epitopes; synthesis and identification of bivalent binding RNA mols. to G protein-coupled receptors)

INDEX TERM: Epitopes  
    (of G protein-coupled receptors; synthesis and identification of bivalent binding RNA mols. to G protein-coupled receptors)

INDEX TERM: Thyrotropin receptors  
ROLE: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)  
    (of canine/rat or human, screening for bivalent nuclear acid ligands binding to peptides of; synthesis and identification of bivalent binding RNA mols. to G protein-coupled receptors)

INDEX TERM: Gonadotropin-releasing hormone receptor  
VIP receptors  
ROLE: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)  
    (of human, screening for bivalent nuclear acid ligands binding to peptides of; synthesis and identification of bivalent binding RNA mols. to G protein-coupled receptors)

INDEX TERM: Gonadotropin receptors  
ROLE: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)  
    (of human/rat/mouse, screening for bivalent nuclear acid ligands binding to peptides of; synthesis and identification of bivalent binding RNA mols. to G

INDEX TERM: protein-coupled receptors)  
Calcitonin receptors  
ROLE: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)  
(of human/rat/pig, screening for bivalent nuclear acid ligands binding to peptides of; synthesis and identification of bivalent binding RNA mols. to G protein-coupled receptors)

INDEX TERM: Corticotropin releasing factor receptors  
Glucagon receptors  
Growth hormone-releasing hormone receptors  
Neuropeptide Y receptors  
ROLE: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)  
(of rat, screening for bivalent nuclear acid ligands binding to peptides of; synthesis and identification of bivalent binding RNA mols. to G protein-coupled receptors)

INDEX TERM: Muscarinic receptors  
ROLE: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)  
(of swine or Drosophila, screening for bivalent nuclear acid ligands binding to; synthesis and identification of bivalent binding RNA mols. to G protein-coupled receptors)

INDEX TERM: Affinity chromatography  
(screening for bivalent ligand to G protein-coupled receptors epitopes; synthesis and identification of bivalent binding RNA mols. to G protein-coupled receptors)

INDEX TERM: G protein-coupled receptors  
ROLE: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)  
(synthesis and identification of bivalent binding RNA mols. to G protein-coupled receptors)

INDEX TERM: Polysiloxanes, biological studies  
ROLE: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)  
(thio or carboxy-functionalized, **aptamers** linked by; synthesis and identification of bivalent binding RNA mols. to G protein-coupled receptors)

INDEX TERM: PCR (polymerase chain reaction)  
(to link G protein coupled receptor epitope ECL1- or ECL2-binding RNA mols.; synthesis and identification of bivalent binding RNA mols. to G protein-coupled receptors)

INDEX TERM: Opioid receptors  
ROLE: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)  
( $\kappa$ -opioid, of human/rat/mouse, screening for bivalent nuclear acid ligands binding to; synthesis and identification of bivalent binding RNA mols. to G protein-coupled receptors)

INDEX TERM: Adrenoceptors  
ROLE: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)  
( $\alpha_1$ , of hamster or bovine, screening for bivalent nuclear acid ligands binding to; synthesis and identification of bivalent binding RNA mols. to G protein-coupled receptors)

INDEX TERM: Adrenoceptors  
ROLE: BUU (Biological use, unclassified); BIOL (Biological

INDEX TERM: Adrenoceptors  
ROLE: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)  
( $\alpha$ 1D, of rat, screening for bivalent nuclear acid ligands binding to; synthesis and identification of bivalent binding RNA mols. to G protein-coupled receptors)

INDEX TERM: Adrenoceptors  
ROLE: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)  
( $\alpha$ 2, D, of human or rat, screening for bivalent nuclear acid ligands binding to; synthesis and identification of bivalent binding RNA mols. to G protein-coupled receptors)

INDEX TERM: Adrenoceptors  
ROLE: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)  
( $\alpha$ 2, of human or mouse or fish, screening for bivalent nuclear acid ligands binding to; synthesis and identification of bivalent binding RNA mols. to G protein-coupled receptors)

INDEX TERM: Adrenoceptors  
ROLE: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)  
( $\alpha$ 2A, of human or porcine or rat, screening for bivalent nuclear acid ligands binding to; synthesis and identification of bivalent binding RNA mols. to G protein-coupled receptors)

INDEX TERM: Adrenoceptors  
ROLE: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)  
( $\alpha$ 2B, of human or rat, screening for bivalent nuclear acid ligands binding to; synthesis and identification of bivalent binding RNA mols. to G protein-coupled receptors)

INDEX TERM: Adrenoceptors  
ROLE: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)  
( $\alpha$ 2C, of mouse or rat, screening for bivalent nuclear acid ligands binding to; synthesis and identification of bivalent binding RNA mols. to G protein-coupled receptors)

INDEX TERM: Adrenoceptors  
ROLE: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)  
( $\beta$ 1, of rat or human or mouse, screening for bivalent nuclear acid ligands binding to; synthesis and identification of bivalent binding RNA mols. to G protein-coupled receptors)

INDEX TERM: Adrenoceptors  
ROLE: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)  
( $\beta$ 2, of rat or human or mouse, screening for bivalent nuclear acid ligands binding to; synthesis and identification of bivalent binding RNA mols. to G protein-coupled receptors)

INDEX TERM: Adrenoceptors  
ROLE: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)  
( $\beta$ 3, of rat or human or bovine, screening for bivalent nuclear acid ligands binding to; synthesis and identification of bivalent binding RNA mols. to G protein-coupled receptors)

INDEX TERM: Opioid receptors

INDEX TERM: ROLE: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)  
( $\delta$ -opioid, of human/mouse, screening for bivalent nuclear acid ligands binding to; synthesis and identification of bivalent binding RNA mols. to G protein-coupled receptors)

INDEX TERM: Opioid receptors  
ROLE: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)  
( $\mu$ -opioid, of human/rat, screening for bivalent nuclear acid ligands binding to; synthesis and identification of bivalent binding RNA mols. to G protein-coupled receptors)

INDEX TERM: 79-10-7D, 2-Propenoic acid, polymers 9002-89-5  
9004-53-9, Dextrin 12619-70-4, Cyclodextrin 25322-68-3  
25322-69-4  
ROLE: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)  
(aptamers linked by; synthesis and identification of bivalent binding RNA mols. to G protein-coupled receptors)

INDEX TERM: 268720-50-9P, RNA (synthetic)  
ROLE: BAC (Biological activity or effector, except adverse); BPN (Biosynthetic preparation); BSU (Biological study, unclassified); PUR (Purification or recovery); BIOL (Biological study); PREP (Preparation)  
(as ligands to G protein coupled-receptor; synthesis and identification of bivalent binding RNA mols. to G protein-coupled receptors)

INDEX TERM: 255916-21-3 255916-22-4  
ROLE: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)  
(neurokinin receptor 1 NK1R epitope; synthesis and identification of bivalent binding RNA mols. to G protein-coupled receptors)

REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD.

REFERENCE(S): (1) Bracht; US 5780449 A 1998 CAPLUS  
(2) Gold; US 5270163 A 1993 CAPLUS  
(3) Nieuwlandt; US 5648214 A 1997 CAPLUS  
(4) Xu, W; Proc Natl Acad Sci USA 1996, V93, P7475 CAPLUS

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=> d 1-17 111 iall
YOU HAVE REQUESTED DATA FROM FILE 'EMBASE, BIOSIS, SCISEARCH, MEDLINE, CAPLUS' -
CONTINUE? (Y)/N:
YOU HAVE REQUESTED DATA FROM FILE 'EMBASE, BIOSIS, SCISEARCH, MEDLINE, CAPLUS' -
CONTINUE? (Y)/N:y
```

L11 ANSWER 1 OF 17 EMBASE COPYRIGHT 2005 ELSEVIER INC. ALL RIGHTS RESERVED.  
on STN  
ACCESSION NUMBER: 2003152968 EMBASE  
TITLE: Yeast genetic selections to optimize RNA decoys for  
transcription factor NF- $\kappa$ B.  
AUTHOR: Cassiday L.A.; Maher III L.J.  
CORPORATE SOURCE: L.J. Maher III, Department of Biochemistry, Mayo  
Foundation, 200 First Street SW, Rochester, MN 55905,  
United States. maher@mayo.edu  
SOURCE: Proceedings of the National Academy of Sciences of the

United States of America, (1 Apr 2003) Vol. 100, No. 7, pp. 3930-3935.  
Refs: 25  
ISSN: 0027-8424 CODEN: PNASA6

COUNTRY: United States  
DOCUMENT TYPE: Journal; Article  
FILE SEGMENT: 004 Microbiology  
LANGUAGE: English  
SUMMARY LANGUAGE: English  
ENTRY DATE: Entered STN: 20030501  
Last Updated on STN: 20030501

**ABSTRACT:** In vitro-selected RNA **aptamers** are potential inhibitors of disease-related proteins. Our laboratory previously isolated an RNA \*\*\*aptamer\*\*\* that binds with high affinity to human transcription factor NF- $\kappa$ B. This RNA **aptamer** competitively inhibits DNA binding by NF- $\kappa$ B in vitro and is recognized by its target protein in vivo in a yeast three-hybrid system. In the present study, yeast genetic selections were used to optimize the RNA **aptamer** for binding to NF- $\kappa$ B in the eukaryotic nucleus. Selection for improved binding to NF- $\kappa$ B from RNA libraries encoding (i) degenerate **aptamer** variants and (ii) sequences present at round 8 of 14 total rounds of in vitro selection yielded RNA \*\*\*aptamers\*\*\* with dramatically improved in vivo activity. Furthermore, we show that an in vivo-optimized RNA **aptamer** exhibits specific "decoy" activity, inhibiting transcriptional activation by its NF- $\kappa$ B target protein in a yeast one-hybrid assay. This decoy activity is enhanced by the expression of a **bivalent aptamer**. The combination of in vitro and in vivo genetic selections was crucial for obtaining RNA \*\*\*aptamers\*\*\* with in vivo decoy activity.

CONTROLLED TERM: Medical Descriptors:  
\*genetic selection  
yeast  
protein isolation  
DNA binding  
competitive inhibition  
eukaryotic cell  
cell nucleus  
RNA sequence  
protein function  
transcription regulation  
gene expression regulation  
nonhuman  
article  
priority journal  
Drug Descriptors:  
\*RNA  
\*immunoglobulin enhancer binding protein  
\*aptamer  
DNA

CAS REGISTRY NO.: (RNA) 63231-63-0; (DNA) 9007-49-2

L11 ANSWER 2 OF 17 EMBASE COPYRIGHT 2005 ELSEVIER INC. ALL RIGHTS RESERVED.  
on STN

ACCESSION NUMBER: 1998397104 EMBASE  
TITLE: Anti-L-selectin oligonucleotide ligands recognize CD62L-positive leukocytes: Binding affinity and specificity of univalent and bivalent ligands.  
AUTHOR: Ringquist S.; Parma D.  
CORPORATE SOURCE: D. Parma, NeXstar Pharmaceuticals, Inc., 2860 Wilderness Place, Boulder, CO 80301, United States. parma@nexstar.com  
SOURCE: Cytometry, (1 Dec 1998) Vol. 33, No. 4, pp. 394-405.  
Refs: 81

ISSN: 0196-4763 CODEN: CYTODQ  
COUNTRY: United States  
DOCUMENT TYPE: Journal; Article  
FILE SEGMENT: 027 Biophysics, Bioengineering and Medical  
Instrumentation  
029 Clinical Biochemistry  
LANGUAGE: English  
SUMMARY LANGUAGE: English  
ENTRY DATE: Entered STN: 19981217  
Last Updated on STN: 19981217  
ABSTRACT: Oligonucleotide **aptamers** generated against purified LS-Rg, a human L-selectin/IgG fusion protein, bound human CD62L-positive leukocytes. FACS analysis of lymphocytes or neutrophils stained with fluorescently labeled \*\*\*aptamers\*\*\* indicated specificity and sensitivity for cellular L-selectin similar to that observed with anti-L-selectin antibody. Univalent \*\*\*aptamers\*\*\* were compared to **bivalent aptamers** as well as to the anti-adhesion, anti-L-selectin antibody DREG56. Equilibrium and kinetic binding experiments were performed to examine the affinity and kinetic binding parameters of L-selectin **aptamers** to evaluate their binding to CD62L-positive leukocytes and to test their potential as L-selectin antagonists. Binding experiments indicated that **bivalent aptamers** approached the affinity and the dissociation rate of **bivalent antibody**, and preferentially recognized cellular compared to soluble L-selectin, a potentially useful distinction *in vivo*. Anti-L-selectin \*\*\*aptamers\*\*\* also inhibited L-selectin dependent self-adhesion of neutrophils suggesting that *in vitro* univalent and **bivalent aptamers** provided anti-adhesion activity similar to that observed with blocking antibody and indicated a direct blocking mechanism of action during inhibition of L-selectin-dependent trafficking of lymphocytes observed *in vivo*.  
CONTROLLED TERM: Medical Descriptors:  
\*flow cytometry  
\*leukocyte adherence  
ligand binding  
antigen recognition  
binding affinity  
fluorescence microscopy  
dissociation constant  
neutrophil chemotaxis  
lymphocyte subpopulation  
human  
controlled study  
human cell  
article  
priority journal  
Drug Descriptors:  
\*l selectin: EC, endogenous compound  
\*padgem protein  
\*hybrid protein: EC, endogenous compound  
selectin antagonist  
l selectin antibody  
okt 8  
monoclonal antibody cd11b  
monoclonal antibody cd 20  
okt 4  
monoclonal antibody cd 62  
unclassified drug  
CAS REGISTRY NO.: (l selectin) 126880-86-2

DOCUMENT NUMBER: PREV200300252273  
TITLE: Yeast genetic selections to optimize RNA decoys for transcription factor NF-kappaB.  
AUTHOR(S): Cassiday, Laura A.; Maher, L. James III [Reprint Author]  
CORPORATE SOURCE: Department of Biochemistry and Molecular Biology, Mayo Foundation, 200 First Street SW, Guggenheim 16, Rochester, MN, 55905, USA  
maher@mayo.edu  
SOURCE: Proceedings of the National Academy of Sciences of the United States of America, (April 1 2003) Vol. 100, No. 7, pp. 3930-3935. print.  
ISSN: 0027-8424 (ISSN print).  
DOCUMENT TYPE: Article  
LANGUAGE: English  
ENTRY DATE: Entered STN: 28 May 2003  
Last Updated on STN: 28 May 2003  
ABSTRACT: In vitro-selected RNA **aptamers** are potential inhibitors of disease-related proteins. Our laboratory previously isolated an RNA \*\*\*aptamer\*\*\* that binds with high affinity to human transcription factor NF-kappaB. This RNA **aptamer** competitively inhibits DNA binding by NF-kappaB in vitro and is recognized by its target protein in vivo in a yeast three-hybrid system. In the present study, yeast genetic selections were used to optimize the RNA **aptamer** for binding to NF-kappaB in the eukaryotic nucleus. Selection for improved binding to NF-kappaB from RNA libraries encoding (i) degenerate **aptamer** variants and (ii) sequences present at round 8 of 14 total rounds of in vitro selection yielded RNA \*\*\*aptamers\*\*\* with dramatically improved in vivo activity. Furthermore, we show that an in vivo-optimized RNA **aptamer** exhibits specific "decoy" activity, inhibiting transcriptional activation by its NF-kappaB target protein in a yeast one-hybrid assay. This decoy activity is enhanced by the expression of a **bivalent aptamer**. The combination of in vitro and in vivo genetic selections was crucial for obtaining RNA **aptamers** with in vivo decoy activity.  
CONCEPT CODE: Genetics - General 03502  
Genetics - Plant 03504  
Biochemistry studies - Nucleic acids, purines and pyrimidines 10062  
Biochemistry studies - Proteins, peptides and amino acids 10064  
Pathology - Therapy 12512  
Pharmacology - General 22002  
INDEX TERMS: Major Concepts  
Methods and Techniques; Molecular Genetics (Biochemistry and Molecular Biophysics); Pharmacology  
INDEX TERMS: Parts, Structures, & Systems of Organisms  
nucleus  
INDEX TERMS: Chemicals & Biochemicals  
DNA: transcription inhibition; NF-kappa-B [nuclear factor-kappa-B]; RNA: pharmaceutical  
INDEX TERMS: Methods & Equipment  
RNA engineering: laboratory techniques; genetic selection: genetic techniques, laboratory techniques; yeast one-hybrid assay: genetic techniques, laboratory techniques; yeast three-hybrid assay: genetic techniques, laboratory techniques  
ORGANISM: Classifier  
Fungi 15000  
Super Taxa  
Plantae  
Organism Name  
yeast (common)  
Taxa Notes

Fungi, Microorganisms, Nonvascular Plants, Plants

L11 ANSWER 4 OF 17 BIOSIS COPYRIGHT (c) 2005 The Thomson Corporation on STN  
ACCESSION NUMBER: 1999:28644 BIOSIS  
DOCUMENT NUMBER: PREV199900028644  
TITLE: Anti-L-selectin oligonucleotide ligands recognize  
CD62L-positive leukocytes: Binding affinity and specificity  
of univalent and **bivalent** ligands.  
AUTHOR(S): Ringquist, Steven; Parma, David [Reprint author]  
CORPORATE SOURCE: NeXstar Pharmaceuticals Inc., 2860 Wilderness Place, Suite  
200, Boulder, CO 80301, USA  
SOURCE: Cytometry, (Dec. 1, 1998) Vol. 33, No. 4, pp. 394-405.  
print.  
CODEN: CYTODQ. ISSN: 0196-4763.  
DOCUMENT TYPE: Article  
LANGUAGE: English  
ENTRY DATE: Entered STN: 3 Feb 1999  
Last Updated on STN: 3 Feb 1999  
ABSTRACT: Oligonucleotide **aptamers** generated against purified LS-Rg, a  
human L-selectin/IgG fusion protein, bound human CD62L positive leukocytes.  
FACS analysis of lymphocytes or neutrophils stained with fluorescently labeled  
\*\*\*aptamers\*\*\* indicated specificity and sensitivity for cellular L-selectin  
similar to that observed with anti-L-selectin antibody. Univalent  
\*\*\*aptamers\*\*\* were compared to **bivalent aptamers** as well  
as to the anti-adhesion, anti-selectin antibody DREG56. Equilibrium and  
kinetic binding experiments were performed to examine the affinity and kinetic  
binding parameters of L-selectin **aptamers** to evaluate their binding  
to CD62L-positive leukocytes and to test their potential as L-selectin  
antagonists. Binding experiments indicated that **bivalent**  
\*\*\*aptamers\*\*\* approached the affinity and the dissociation rate of  
\*\*\*bivalent\*\*\* antibody, and preferentially recognized cellular compared to  
soluble L-selectin, a potentially useful distinction in vivo. Anti-selectin  
\*\*\*aptamers\*\*\* also inhibited L-selectin dependent self-adhesion of  
neutrophils suggesting that in vitro univalent and **bivalent**  
\*\*\*aptamers\*\*\* provided anti-adhesion activity similar to that observed with  
blocking antibody and indicated a direct blocking mechanism of action during  
inhibition of L-selectin-dependent trafficking of lymphocytes observed in vivo.  
CONCEPT CODE: Biophysics - Methods and techniques 10504  
Cytology - Human 02508  
Immunology - General and methods 34502  
Biochemistry studies - Nucleic acids, purines and  
pyrimidines 10062  
Biochemistry studies - Proteins, peptides and amino acids  
10064  
INDEX TERMS: Major Concepts  
Cell Biology; Methods and Techniques  
INDEX TERMS: Parts, Structures, & Systems of Organisms  
CD62L-positive leukocytes: blood and lymphatics, immune  
system  
INDEX TERMS: Chemicals & Biochemicals  
anti-L-selectin **aptamers**; anti-L-selectin  
oligonucleotide ligands; DREG56: anti-L-selectin  
antibody  
INDEX TERMS: Methods & Equipment  
flow cytometry: analytical method, cytophotometry: CT;  
neutrophil-neutrophil adhesion assay:  
Analysis/Characterization Techniques: CT, analytical  
method; nitrocellulose filter binding assay: analytical  
method, binding assays; FACSCalibur fluorescence  
activated cell sorter: equipment  
ORGANISM: Classifier  
Hominidae 86215

Super Taxa  
 Primates; Mammalia; Vertebrata; Chordata; Animalia  
 Organism Name  
 human  
 Taxa Notes  
 Animals, Chordates, Humans, Mammals, Primates,  
 Vertebrates  
 REGISTRY NUMBER: 9004-70-0 (NITROCELLULOSE)

L11 ANSWER 5 OF 17 SCISEARCH COPYRIGHT (c) 2005 The Thomson Corporation on  
 STN  
 ACCESSION NUMBER: 2003:320652 SCISEARCH  
 THE GENUINE ARTICLE: 664JR  
 TITLE: Yeast genetic selections to optimize RNA decoys for  
 transcription factor NF-kappa B  
 AUTHOR: Cassiday L A; Maher L J (Reprint)  
 CORPORATE SOURCE: Mayo Clin & Mayo Fdn, Dept Biochem & Mol Biol, 200 1st St  
 SW, Guggenheim 16, Rochester, MN 55905 USA (Reprint); Mayo  
 Clin & Mayo Fdn, Dept Biochem & Mol Biol, Rochester, MN  
 55905 USA  
 COUNTRY OF AUTHOR: USA  
 SOURCE: PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF THE  
 UNITED STATES OF AMERICA, (1 APR 2003) Vol. 100, No. 7,  
 pp. 3930-3935.  
 Publisher: NATL ACAD SCIENCES, 2101 CONSTITUTION AVE NW,  
 WASHINGTON, DC 20418 USA.  
 ISSN: 0027-8424.

DOCUMENT TYPE: Article; Journal

LANGUAGE: English

REFERENCE COUNT: 25

ABSTRACT:

In vitro-selected RNA **aptamers** are potential inhibitors of  
 disease-related proteins. Our laboratory previously isolated an RNA  
 \*\*\*aptamer\*\*\* that binds with high affinity to human transcription factor  
 NF-kappaB. This RNA **aptamer** competitively inhibits DNA binding by  
 NF-kappaB in vitro and is recognized by its target protein in vivo in a yeast  
 three-hybrid system. In the present study, yeast genetic selections were used  
 to optimize the RNA **aptamer** for binding to NF-kappaB in the  
 eukaryotic nucleus. Selection for improved binding to NF-kappaB from RNA  
 libraries encoding (f) degenerate **aptamer** variants and (6) sequences  
 present at round 8 of 14 total rounds of in vitro selection yielded RNA  
 \*\*\*aptamers\*\*\* with dramatically improved in vivo activity. Furthermore, we  
 show that an in vivo-optimized RNA **aptamer** exhibits specific "decoy"  
 activity, inhibiting transcriptional activation by its NF-kappaB target protein  
 in a yeast one-hybrid assay. This decoy activity is enhanced by the expression  
 of a **bivalent aptamer**. The combination of in vitro and in  
 vivo genetic selections was crucial for obtaining RNA **aptamers** with  
 in vivo decoy activity.

CATEGORY: MULTIDISCIPLINARY SCIENCES

SUPPL. TERM PLUS: SACCHAROMYCES-CEREVISIAE; IN-VIVO; FACTOR TARGET;  
**APTAMER**; DNA; INHIBITION; ACTIVATION; SITE

REFERENCE(S):

Referenced Author (RAU)	Year	VOL	ARN PG	Referenced Work (RWP)
*CLONTECH	1999	1	34	YEAST PROT HDB
BAEUEERLE P A	1996	187	13	CELL
BEG A A	1996	1274	1782	SCIENCE
BLIND M	1999	196	13606	P NATL ACAD SCI USA
CAHIRMCFARLAND E D	2000	197	16055	P NATL ACAD SCI USA
CAPONIGRO G	1993	13	15141	MOL CELL BIOL

CASSIDAY L A	2002  30	4118	NUCLEIC ACIDS RES
CASSIDAY L A	2001  40	2433	BIOCHEMISTRY-US
CASSIDAY L A	2002  306	290	ANAL BIOCHEM
ERHART E	1983  156	625	J BACTERIOL
FUJITA T	1992  6	775	GENE DEV
GHOSH G	1995  373	303	NATURE
HANNON G J	2002  418	244	NATURE
ISHIZAKI J	1996  2	1386	NAT MED
JAEGER J A	1990  183	281	METHOD ENZYML
JAEGER J A	1989  86	7706	P NATL ACAD SCI USA
KUNSCH C	1992  12	4412	MOL CELL BIOL
LEBRUSKA L L	1999  38	3168	BIOCHEMISTRY-US
MARTELL R E	2002  6	30	MOL THER
MORISHITA R	1997  3	894	NAT MED
SENGUPTA D J	1996  93	8496	P NATL ACAD SCI USA
SHI H	1999  96	10033	P NATL ACAD SCI USA
SULLENGER B A	2002  418	252	NATURE
ZHANG X T	2001  276	47844	J BIOL CHEM
ZUKER M	1989  244	48	SCIENCE

L11 ANSWER 6 OF 17 SCISEARCH COPYRIGHT (c) 2005 The Thomson Corporation on STN

ACCESSION NUMBER: 1998:904343 SCISEARCH

THE GENUINE ARTICLE: 141GR

TITLE: Anti-L-selectin oligonucleotide ligands recognize CD62L-positive leukocytes: Binding affinity and specificity of univalent and **bivalent** ligands

AUTHOR: Ringquist S; Parma D (Reprint)

CORPORATE SOURCE: NEXSTAR PHARMACEUT INC, 2860 WILDERNESS PL, SUITE 200, BOULDER, CO 80301 (Reprint); NEXSTAR PHARMACEUT INC, BOULDER, CO 80301

COUNTRY OF AUTHOR: USA

SOURCE: CYTOMETRY, (1 DEC 1998) Vol. 33, No. 4, pp. 394-405. Publisher: WILEY-LISS, DIV JOHN WILEY & SONS INC, 605 THIRD AVE, NEW YORK, NY 10158-0012.

ISSN: 0196-4763.

DOCUMENT TYPE: Article; Journal

FILE SEGMENT: LIFE

LANGUAGE: English

REFERENCE COUNT: 81

ABSTRACT:

Oligonucleotide **aptamers** generated against purified LS-Rg, a human L-selectin/IgG fusion protein, bound human CD62L-positive leukocytes. FAGS analysis of lymphocytes or neutrophils stained with fluorescently labeled \*\*\*aptamers\*\*\* indicated specificity and sensitivity for cellular L-selectin similar to that observed with anti-L-selectin antibody. Univalent \*\*\*aptamers\*\*\* were compared to **bivalent aptamers** as well as to the anti-adhesion, anti-L-selectin antibody DREG56. Equilibrium and kinetic binding experiments were performed. to examine the affinity acid kinetic binding parameters of L-selectin **aptamers** to evaluate their binding to CD62L-positive leukocytes and to test their potential as L-selectin antagonists. Binding experiments indicated that **bivalent** \*\*\*aptamers\*\*\* approached the affinity and the dissociation rate of \*\*\*bivalent\*\*\* antibody, and preferentially recognized cellular compared to soluble L-selectin, a potentially useful distinction in vivo. Anti-L-selectin \*\*\*aptamers\*\*\* also inhibited L-selectin dependent self-adhesion of neutrophils suggesting that in vitro univalent and **bivalent** \*\*\*aptamers\*\*\* provided anti-adhesion activity similar to that observed with blocking antibody and indicated a direct blocking mechanism of action during inhibition of L-selectin-dependent trafficking of lymphocytes observed in vivo. (C) 1998 Wiley-Liss, Inc.

CATEGORY: CELL BIOLOGY; BIOCHEMICAL RESEARCH METHODS  
 SUPPLEMENTARY TERM: adhesion molecules; FAGS staining; cell-to-cell interactions; inflammation  
 SUPPL. TERM PLUS: NODE HOMING RECEPTOR; MEDIATED LUNG INJURY; Q-BETA REPLICASE; RNA LIGANDS; LYMPHOCYTE RECIRCULATION; MONOCLONAL-ANTIBODY; IN-VIVO; CD18-INDEPENDENT ADHESION; EXPONENTIAL ENRICHMENT; NEUTROPHIL AGGREGATION

REFERENCE(S):

Referenced Author (RAU)	Year (RPY)	VOL (RVL)	ARN PG (RPG)	Referenced Work (RWK)
ARBONES M L	1994	1	247	IMMUNITY
BERTOZZI C R	1995	34	14271	BIOCHEMISTRY-US
BRADLEY L M	1994	180	2401	J EXP MED
BROWN D	1995	34	14765	BIOCHEMISTRY-US
BROWN D	1995	34	14775	BIOCHEMISTRY-US
BROWN D	1996	93	11558	P NATL ACAD SCI USA
BUTCHER E C	1996	272	60	SCIENCE
CIESIOLKA J	1995	1	538	RNA
CONNELL G J	1993	32	5497	BIOCHEMISTRY-US
CONNELL G J	1994	264	1137	SCIENCE
CROTHERS D M	1972	9	341	IMMUNOCHEMISTRY
DAILEY M O	1982	128	2134	J IMMUNOL
DAVIS K A	1996	24	702	NUCLEIC ACIDS RES
DELISI C	1981	18	507	MOL IMMUNOL
DELISI C	1980	13	201	Q REV BIOPHYS
DOWER S K	1981	20	6326	BIOCHEMISTRY-US
ELLINGTON A D	1990	346	818	NATURE
GALLATIN W M	1983	304	30	NATURE
GENG J G	1992	267	19846	J BIOL CHEM
GEOFFROY J S	1989	198	2463	J CELL BIOL
GOLD L	1995	64	763	ANNU REV BIOCHEM
GOLD L	1995	270	13581	J BIOL CHEM
HALE S P	1996	93	2755	P NATL ACAD SCI USA
HALLMANN R	1991	174	236	BIOCHEM BIOPH RES CO
HICKE B J	1996	98	2688	J CLIN INVEST
HOU S	1995	155	252	J IMMUNOL
ILLANGASEKARE M	1995	267	643	SCIENCE
IRVINE D	1991	222	739	J MOL BIOL
JAYASENA V K	1996	7	2349	BIOCHEMISTRY-US
JENISON R D	1994	263	1425	SCIENCE
JUNG T M	1988	141	4110	J IMMUNOL
JUTILA M A	1989	143	3318	J IMMUNOL
KANO F M E	1988	140	3701	J IMMUNOL
KANSAS G S	1993	177	833	J EXP MED
KANSAS G S	1985	134	2995	J IMMUNOL
KAUFMAN E N	1992	52	4157	CANCER RES
KISHIMOTO T K	1991	78	805	BLOOD
KISHIMOTO T K	1990	87	2244	P NATL ACAD SCI USA
KISHIMOTO T K	1989	245	1238	SCIENCE
KLOTZ I M	1985	18	227	Q REV BIOPHYS
LEWINSOHN D M	1987	138	4313	J IMMUNOL
LEY K	1991	77	2553	BLOOD
LEY K	1993	82	1632	BLOOD
LEY K	1995	181	669	J EXP MED
LEY K	1995	155	525	J IMMUNOL
LIPKIN E W	1986	261	1702	J BIOL CHEM
LUSCINSKAS F W	1994	125	1417	J CELL BIOL
MA X L	1993	88	649	CIRCULATION
MAYO K H	1989	264	17838	J BIOL CHEM
MIHELCIC D	1994	84	2322	BLOOD
MULLIGAN M S	1991	88	1396	J CLIN INVEST

MULLIGAN M S	1993	151	6410	J IMMUNOL
MULLIGAN M S	1994	152	832	J IMMUNOL
NAVARRO R F	1985	162	1075	J EXP MED
NIEUWLANDT D	1995	34	5651	BIOCHEMISTRY-US
NORGARD K E	1993	90	1068	P NATL ACAD SCI USA
OCONNELL D	1996	93	5883	P NATL ACAD SCI USA
PICKER L J	1993	150	1105	J IMMUNOL
POLLET R J	1977	252	5828	J BIOL CHEM
REICHERT R A	1983	157	813	J EXP MED
REYNOLDS J A	1979	18	264	BIOCHEMISTRY-US
RIGGS A D	1970	53	401	J MOL BIOL
RINGQUIST S	1993	32	10254	BIOCHEMISTRY-US
RINGQUIST S	1995	34	3640	BIOCHEMISTRY-US
SCHNEIDER D	1992	228	862	J MOL BIOL
SIMON S I	1993	82	1097	BLOOD
SIMON S I	1990	111	2747	J CELL BIOL
SIMON S I	1992	149	2765	J IMMUNOL
SPERTINI O	1991	5	300	LEUKEMIA
SPERTINI O	1991	349	691	NATURE
SPRINGER T A	1995	57	827	ANNU REV PHYSIOL
TEDDER T F	1995	9	866	FASEB J
TEDDER T F	1995	181	2259	J EXP MED
TEDDER T F	1990	144	532	J IMMUNOL
TUERK C	1990	249	505	SCIENCE
VONANDRIAN U H	1992	263	H1034	AM J PHYSIOL
VONANDRIAN U H	1993	91	2893	J CLIN INVEST
VONANDRIAN U H	1991	87	7538	P NATL ACAD SCI USA
WATSON S R	1991	349	164	NATURE
YARUS M	1969	42	171	J MOL BIOL
YEDNOCK T A	1987	104	725	J CELL BIOL

L11 ANSWER 7 OF 17

MEDLINE on STN

ACCESSION NUMBER: 2003155336 MEDLINE  
 DOCUMENT NUMBER: PubMed ID: 12637683  
 TITLE: Yeast genetic selections to optimize RNA decoys for transcription factor NF-kappa B.  
 AUTHOR: Cassiday Laura A; Maher L James 3rd  
 CORPORATE SOURCE: Department of Biochemistry and Molecular Biology, Mayo Foundation, Rochester, MN 55905, USA.  
 SOURCE: Proceedings of the National Academy of Sciences of the United States of America, (2003 Apr 1) 100 (7) 3930-5.  
 Electronic Publication: 2003-03-13.  
 Journal code: 7505876. ISSN: 0027-8424.  
 PUB. COUNTRY: United States  
 DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)  
 LANGUAGE: English  
 FILE SEGMENT: Priority Journals  
 ENTRY MONTH: 200305  
 ENTRY DATE: Entered STN: 20030403  
 Last Updated on STN: 20030523  
 Entered Medline: 20030522

ABSTRACT:

In vitro-selected RNA **aptamers** are potential inhibitors of disease-related proteins. Our laboratory previously isolated an RNA **aptamer** that binds with high affinity to human transcription factor NF-kappaB. This RNA **aptamer** competitively inhibits DNA binding by NF-kappaB in vitro and is recognized by its target protein in vivo in a yeast three-hybrid system. In the present study, yeast genetic selections were used to optimize the RNA **aptamer** for binding to NF-kappaB in the eukaryotic nucleus. Selection for improved binding to NF-kappaB from RNA libraries encoding (i) degenerate **aptamer** variants and (ii) sequences present at round 8 of 14 total rounds of in vitro selection yielded RNA

\*\*\*aptamers\*\*\* with dramatically improved in vivo activity. Furthermore, we show that an in vivo-optimized RNA **aptamer** exhibits specific "decoy" activity, inhibiting transcriptional activation by its NF-kappaB target protein in a yeast one-hybrid assay. This decoy activity is enhanced by the expression of a **bivalent aptamer**. The combination of in vitro and in vivo genetic selections was crucial for obtaining RNA **aptamers** with in vivo decoy activity.

CONTROLLED TERM:      Base Sequence  
                         Cloning, Molecular  
                         Kinetics  
                         Molecular Sequence Data  
\*NF-kappa B: ME, metabolism  
                         Nucleic Acid Conformation  
                         RNA, Fungal: CH, chemistry  
\*RNA, Fungal: GE, genetics  
                         RNA, Fungal: ME, metabolism  
                         Research Support, Non-U.S. Gov't  
\*Saccharomyces cerevisiae: GE, genetics  
                         Saccharomyces cerevisiae Proteins: GE, genetics  
\*Selection (Genetics)  
CHEMICAL NAME:      0 (NF-kappa B); 0 (RNA, Fungal); 0 (Saccharomyces cerevisiae Proteins)

L11 ANSWER 8 OF 17      MEDLINE on STN  
ACCESSION NUMBER:      1999059566      MEDLINE  
DOCUMENT NUMBER:      PubMed ID: 9845433  
TITLE:      Anti-L-selectin oligonucleotide ligands recognize CD62L-positive leukocytes: binding affinity and specificity of univalent and **bivalent** ligands.  
AUTHOR:      Ringquist S; Parma D  
CORPORATE SOURCE:      NeXstar Pharmaceuticals, Inc., Boulder, Colorado 80301, USA.  
SOURCE:      Cytometry : journal of the Society for Analytical Cytology, (1998 Dec 1) 33 (4) 394-405.  
                         Journal code: 8102328. ISSN: 0196-4763.  
PUB. COUNTRY:      United States  
DOCUMENT TYPE:      Journal; Article; (JOURNAL ARTICLE)  
LANGUAGE:      English  
FILE SEGMENT:      Priority Journals  
ENTRY MONTH:      199902  
ENTRY DATE:      Entered STN: 19990223  
                         Last Updated on STN: 19990223  
                         Entered Medline: 19990211

ABSTRACT:  
Oligonucleotide **aptamers** generated against purified LS-Rg, a human L-selectin/IgG fusion protein, bound human CD62L-positive leukocytes. FACS analysis of lymphocytes or neutrophils stained with fluorescently labeled \*\*\*aptamers\*\*\* indicated specificity and sensitivity for cellular L-selectin similar to that observed with anti-L-selectin antibody. Univalent \*\*\*aptamers\*\*\* were compared to **bivalent aptamers** as well as to the anti-adhesion, anti-L-selectin antibody DREG56. Equilibrium and kinetic binding experiments were performed to examine the affinity and kinetic binding parameters of L-selectin **aptamers** to evaluate their binding to CD62L-positive leukocytes and to test their potential as L-selectin antagonists. Binding experiments indicated that **bivalent** \*\*\*aptamers\*\*\* approached the affinity and the dissociation rate of \*\*\*bivalent\*\*\* antibody, and preferentially recognized cellular compared to soluble L-selectin, a potentially useful distinction in vivo. Anti-L-selectin \*\*\*aptamers\*\*\* also inhibited L-selectin dependent self-adhesion of neutrophils suggesting that in vitro univalent and **bivalent** \*\*\*aptamers\*\*\* provided anti-adhesion activity similar to that observed with blocking antibody and indicated a direct blocking mechanism of action during

inhibition of L-selectin-dependent trafficking of lymphocytes observed in vivo.

CONTROLLED TERM: Base Sequence

Cell Adhesion

Humans

Kinetics

\*L-Selectin: AN, analysis

L-Selectin: IM, immunology

\*Leukocytes: IM, immunology

Ligands

Lymphocytes: IM, immunology

Molecular Sequence Data

Neutrophils: IM, immunology

Neutrophils: ME, metabolism

\*Oligonucleotides: IM, immunology

Solubility

Staining and Labeling

CAS REGISTRY NO.: 126880-86-2 (L-Selectin)

CHEMICAL NAME: 0 (Ligands); 0 (Oligonucleotides)

L11 ANSWER 9 OF 17 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2005:48600 CAPLUS

DOCUMENT NUMBER: 142:312421

ENTRY DATE: Entered STN: 20 Jan 2005

TITLE: Nucleic Acid-Based Fluorescence Sensors for Detecting Proteins

AUTHOR(S): Heyduk, Ewa; Heyduk, Tomasz

CORPORATE SOURCE: Edward A. Doisy Department of Biochemistry and Molecular Biology, St. Louis University Medical School, St. Louis, MO, 63104, USA

SOURCE: Analytical Chemistry (2005), 77(4), 1147-1156

CODEN: ANCHAM; ISSN: 0003-2700

PUBLISHER: American Chemical Society

DOCUMENT TYPE: Journal

LANGUAGE: English

CLASSIFICATION: 9-5 (Biochemical Methods)  
Section cross-reference(s): 3

ABSTRACT:

We report here development of a rapid, homogeneous, aptamer-based fluorescence assay ("mol. beacons") for detecting proteins. The assay involves protein-induced coassocn. of two aptamers recognizing two distinct epitopes of the protein. The aptamers contain short fluorophore-labeled complementary "signaling" oligonucleotides attached to the \*\*\*aptamer\*\*\* by non-DNA linker. Coassocn. of the two aptamers with the protein results in bringing the two "signaling" oligonucleotides into proximity, producing a large change of fluorescence resonance energy transfer between the fluorophores. We used thrombin as a model system to provide proof-of-principle evidence validating this mol. beacon design. Thrombin beacon was capable of detecting the protein with high selectivity (also in complex biol. mixts.), picomolar sensitivity, and high signal-to-background ratio. This is a homogeneous assay requiring no sample manipulation. Since the design of mol. beacons described here is not limited to any specific protein, it will be possible to develop these beacons to detect a variety of target proteins of biomedical importance.

SUPPL. TERM: aptamer beacon FRET detection protein thrombin model; fluorescence resonance energy transfer detection protein

INDEX TERM: Proteins

ROLE: ANT (Analyte); ANST (Analytical study)  
(DNA-binding; nucleic acid-based fluorescence sensors for detecting proteins)

INDEX TERM: Oligonucleotides

ROLE: ARU (Analytical role, unclassified); BUU (Biological use, unclassified); ANST (Analytical study); BIOL (Biological study); USES (Uses)  
(attached to the **aptamer** by non-DNA linker;  
nucleic acid-based fluorescence sensors for detecting proteins)

INDEX TERM: **Aptamers**  
(bivalent thrombin, attached to  
oligonucleotides by non-DNA linker; nucleic acid-based fluorescence sensors for detecting proteins)

INDEX TERM: Biosensors  
Electrophoresis  
Fluorescence  
Fluorescence resonance energy transfer  
Fluorometry  
(nucleic acid-based fluorescence sensors for detecting proteins)

INDEX TERM: 2321-07-5, Fluorescein 6268-49-1, Dabcyl 82354-19-6,  
Texas Red 146368-14-1, Cy5  
ROLE: ARG (Analytical reagent use); BUU (Biological use, unclassified); ANST (Analytical study); BIOL (Biological study); USES (Uses)  
(nucleic acid-based fluorescence sensors for detecting proteins)

INDEX TERM: 9002-04-4, Thrombin  
ROLE: BSU (Biological study, unclassified); BIOL (Biological study)  
(nucleic acid-based fluorescence sensors for detecting proteins)

REFERENCE COUNT: 25 THERE ARE 25 CITED REFERENCES AVAILABLE FOR THIS RECORD.

REFERENCE(S): (1) Bock, L; *Nature* 1992, V355, P564 CAPLUS  
(2) Fang, X; *ChemBioChem* 2003, V4, P829 CAPLUS  
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(9) Heyduk, E; *J Biol Chem* 1997, V272, P19763 CAPLUS  
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(24) Yamamoto, R; *Genes Cells* 2000, V5, P389 CAPLUS  
(25) Zhang, J; *J Biomol Screening* 1999, V4, P67

DOCUMENT NUMBER: 142:49205  
 ENTRY DATE: Entered STN: 17 Dec 2004  
 TITLE: Stabilized **aptamers** to growth factors and  
 their receptors for use in the treatment of solid  
 tumors  
 INVENTOR(S): Epstein, David; Grate, Dilara; Stanton, Martin;  
 Diener, John L.; Wilson, Charles; McCauley, Thomas;  
 DeSouza, Errol  
 PATENT ASSIGNEE(S): USA  
 SOURCE: U.S. Pat. Appl. Publ., 96 pp., Cont.-in-part of U.S.  
 Ser. No. 762,915.  
 CODEN: USXXCO  
 DOCUMENT TYPE: Patent  
 LANGUAGE: English  
 INT. PATENT CLASSIF.:  
     MAIN: C07H021-04  
     SECONDARY: C07K014-705  
 US PATENT CLASSIF.: 435069100; 435320100; 435325000; 530350000; 536023200  
 CLASSIFICATION: 1-6 (Pharmacology)  
 FAMILY ACC. NUM. COUNT: 6  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2004253679	A1	20041216	US 2004-829504	20040421
US 2004180360	A1	20040916	US 2003-718833	20031121
US 2004253243	A1	20041216	US 2004-762915	20040121
PRIORITY APPLN. INFO.:				
			US 2002-428102P	P 20021121
			US 2003-441357P	P 20030121
			US 2003-463095P	P 20030415
			US 2003-464179P	P 20030421
			US 2003-464239P	P 20030421
			US 2003-465053P	P 20030423
			US 2003-465055P	P 20030423
			US 2003-469628P	P 20030508
			US 2003-474133P	P 20030529
			US 2003-474680P	P 20030529
			US 2003-486580P	P 20030711
			US 2003-489810P	P 20030723
			US 2003-491019P	P 20030729
			US 2003-503596P	P 20030916
			US 2003-512071P	P 20031017
			US 2003-718833	A2 20031121
			US 2004-537045P	P 20040116
			US 2004-537201P	P 20040116
			US 2004-762915	A2 20040121

PATENT NO.	CLASS	PATENT FAMILY CLASSIFICATION CODES
US 2004253679	ICM	C07H021-04
	ICS	C07K014-705
	INCL	435069100; 435320100; 435325000; 530350000; 536023200
US 2004253679	NCL	435/069.100; 435/320.100; 435/325.000; 530/350.000; 536/023.200
US 2004180360	NCL	435/006.000; 536/023.500
US 2004253243	NCL	424/145.100

ABSTRACT:

**Aptamers** that bind specifically to platelet-derived growth factor, vascular endothelial growth factor, their receptors and isoforms of the growth factors are described for use in the treatment of solid tumors dependent on these growth factors. They can be used alone or in combination with known cytotoxic agents for the treatment of solid tumors. The **aptamers** are

modified, e.g. by using modified backbones or conjugation with polyethylene glycol, to improve in vivo stability. **Aptamers** with one or more immunostimulant CpG motifs are also described. **Bivalent \*\*\*aptamers\*\*\*** binding one of these targets and another growth- or apoptosis-regulating are also described.

SUPPL. TERM: PDGF VEGF receptor **aptamer** solid tumor cytotoxin therapy

INDEX TERM: Platelet-derived growth factors  
ROLE: BSU (Biological study, unclassified); BIOL (Biological study)  
(AA; stabilized **aptamers** to growth factors and their receptors for use in treatment of solid tumors)

INDEX TERM: Platelet-derived growth factors  
ROLE: BSU (Biological study, unclassified); BIOL (Biological study)  
(AB; stabilized **aptamers** to growth factors and their receptors for use in treatment of solid tumors)

INDEX TERM: CD80 (antigen)  
ROLE: BSU (Biological study, unclassified); BIOL (Biological study)  
(B7-X, **aptamers** for; stabilized **aptamers** to growth factors and their receptors for use in treatment of solid tumors)

INDEX TERM: Cytokines  
ROLE: BSU (Biological study, unclassified); BIOL (Biological study)  
(BAFF, **aptamers** for; stabilized **aptamers** to growth factors and their receptors for use in treatment of solid tumors)

INDEX TERM: Platelet-derived growth factors  
ROLE: BSU (Biological study, unclassified); BIOL (Biological study)  
(BB; stabilized **aptamers** to growth factors and their receptors for use in treatment of solid tumors)

INDEX TERM: Receptors  
ROLE: BSU (Biological study, unclassified); BIOL (Biological study)  
(BTLA (B7x receptors), **aptamers** for; stabilized **aptamers** to growth factors and their receptors for use in treatment of solid tumors)

INDEX TERM: Platelet-derived growth factors  
ROLE: BSU (Biological study, unclassified); BIOL (Biological study)  
(CC and DD isoforms; stabilized **aptamers** to growth factors and their receptors for use in treatment of solid tumors)

INDEX TERM: CD antigens  
ROLE: BSU (Biological study, unclassified); BIOL (Biological study)  
(CD11C, **aptamers** for; stabilized **aptamers** to growth factors and their receptors for use in treatment of solid tumors)

INDEX TERM: CD antigens  
ROLE: BSU (Biological study, unclassified); BIOL (Biological study)  
(CD33, **aptamers** for; stabilized **aptamers** to growth factors and their receptors for use in treatment of solid tumors)

INDEX TERM: Immunostimulants  
(CpG dinucleotide as, in **aptamers**; stabilized **aptamers** to growth factors and their receptors

INDEX TERM: for use in treatment of solid tumors)  
Immunoglobulin receptors  
ROLE: BSU (Biological study, unclassified); BIOL (Biological study)  
(IgE type I, **aptamers** for; stabilized **aptamers** to growth factors and their receptors for use in treatment of solid tumors)

INDEX TERM: Immunoglobulin receptors  
ROLE: BSU (Biological study, unclassified); BIOL (Biological study)  
(IgE type IIb, **aptamers** for; stabilized **aptamers** to growth factors and their receptors for use in treatment of solid tumors)

INDEX TERM: Antibodies and Immunoglobulins  
ROLE: BSU (Biological study, unclassified); BIOL (Biological study)  
(IgE, **aptamers** for; stabilized **aptamers** to growth factors and their receptors for use in treatment of solid tumors)

INDEX TERM: Proteins  
ROLE: BSU (Biological study, unclassified); BIOL (Biological study)  
(PD-L1 (programmed death ligand 1), **aptamers** for; stabilized **aptamers** to growth factors and their receptors for use in treatment of solid tumors)

INDEX TERM: Proteins  
ROLE: BSU (Biological study, unclassified); BIOL (Biological study)  
(PDCD (programmed cell death), PD-1, **aptamers** for; stabilized **aptamers** to growth factors and their receptors for use in treatment of solid tumors)

INDEX TERM: Antigens  
ROLE: BSU (Biological study, unclassified); BIOL (Biological study)  
(PSMA (prostate-specific membrane antigen), **aptamers** for; stabilized **aptamers** to growth factors and their receptors for use in treatment of solid tumors)

INDEX TERM: Genetic methods  
(SELEX, for selection of **aptamers**; stabilized **aptamers** to growth factors and their receptors for use in treatment of solid tumors)

INDEX TERM: Proteins  
ROLE: BSU (Biological study, unclassified); BIOL (Biological study)  
(TIM-3 (T cell Ig- and mucin-domain- containing mol.-3), **aptamers** for; stabilized **aptamers** to growth factors and their receptors for use in treatment of solid tumors)

INDEX TERM: Receptors  
ROLE: BSU (Biological study, unclassified); BIOL (Biological study)  
(TLR (Toll-like receptor), **aptamers** binding growth factors and their receptors and; stabilized **aptamers** to growth factors and their receptors for use in treatment of solid tumors)

INDEX TERM: Cytotoxic agents  
(antimetabolites, cancer therapy with **aptamers** and; stabilized **aptamers** to growth factors and their receptors for use in treatment of solid tumors)

INDEX TERM: CD19 (antigen)  
CD20 (antigen)

CD22 (antigen)  
CTLA-4 (antigen)  
Tumor necrosis factors  
ROLE: BSU (Biological study, unclassified); BIOL (Biological study)  
(aptamers for; stabilized aptamers to  
growth factors and their receptors for use in treatment  
of solid tumors)

INDEX TERM: Alkylating agents, biological  
Angiogenesis inhibitors  
(cancer therapy with aptamers and; stabilized  
aptamers to growth factors and their receptors  
for use in treatment of solid tumors)

INDEX TERM: Nucleoside analogs  
ROLE: THU (Therapeutic use); BIOL (Biological study); USES  
(Uses)  
(cancer therapy with aptamers and; stabilized  
aptamers to growth factors and their receptors  
for use in treatment of solid tumors)

INDEX TERM: Tubulins  
ROLE: BSU (Biological study, unclassified); BIOL (Biological study)  
(cytotoxins acting on, cancer therapy with  
aptamers and; stabilized aptamers to  
growth factors and their receptors for use in treatment  
of solid tumors)

INDEX TERM: Toxins  
ROLE: THU (Therapeutic use); BIOL (Biological study); USES  
(Uses)  
(cytotoxins, cancer therapy with aptamers and;  
stabilized aptamers to growth factors and their  
receptors for use in treatment of solid tumors)

INDEX TERM: Sarcoma  
(fibrosarcoma, dermafibrosarcoma protruberans, therapy  
with aptamers and cytotoxins; stabilized  
aptamers to growth factors and their receptors  
for use in treatment of solid tumors)

INDEX TERM: Neuroglia, neoplasm  
(glioblastoma, therapy with aptamers and  
cytotoxins; stabilized aptamers to growth  
factors and their receptors for use in treatment of solid  
tumors)

INDEX TERM: Oligonucleotides  
ROLE: THU (Therapeutic use); BIOL (Biological study); USES  
(Uses)  
(immunostimulatory, aptamers containing; stabilized  
aptamers to growth factors and their receptors  
for use in treatment of solid tumors)

INDEX TERM: Leukemia  
(myelomonocytic, chronic, therapy with aptamers  
and cytotoxins; stabilized aptamers to growth  
factors and their receptors for use in treatment of solid  
tumors)

INDEX TERM: Animal tissue, disease  
(soft, neoplasm, sarcoma, therapy with aptamers  
and cytotoxins; stabilized aptamers to growth  
factors and their receptors for use in treatment of solid  
tumors)

INDEX TERM: Sarcoma  
(soft-tissue, therapy with aptamers and  
cytotoxins; stabilized aptamers to growth  
factors and their receptors for use in treatment of solid

9

INDEX TERM: tumors)  
 Antitumor agents

INDEX TERM: **Aptamers**  
 (stabilized **aptamers** to growth factors and  
 their receptors for use in treatment of solid tumors)

INDEX TERM: Platelet-derived growth factor receptors  
 Vascular endothelial growth factor receptors  
 ROLE: BSU (Biological study, unclassified); BIOL (Biological study)  
 (stabilized **aptamers** to growth factors and  
 their receptors for use in treatment of solid tumors)

INDEX TERM: Digestive tract, neoplasm  
 (stroma, therapy with **aptamers** and cytotoxins;  
 stabilized **aptamers** to growth factors and their  
 receptors for use in treatment of solid tumors)

INDEX TERM: Interleukin 2 receptors  
 ROLE: BSU (Biological study, unclassified); BIOL (Biological study)  
 ( $\alpha$  chain, **aptamers** for; stabilized  
**aptamers** to growth factors and their receptors  
 for use in treatment of solid tumors)

INDEX TERM: Integrins  
 ROLE: BSU (Biological study, unclassified); BIOL (Biological study)  
 ( $\alpha$ X, **aptamers** for; stabilized  
**aptamers** to growth factors and their receptors  
 for use in treatment of solid tumors)

INDEX TERM: 2382-65-2D, **aptamers** containing  
 ROLE: THU (Therapeutic use); BIOL (Biological study); USES  
 (Uses)  
 (as immunostimulant; stabilized **aptamers** to  
 growth factors and their receptors for use in treatment  
 of solid tumors)

INDEX TERM: 51-21-8, 5-Fluorouracil 59-05-2, Methotrexate 147-94-4,  
 Cytarabine 865-21-4, Vinblastin 15663-27-1, Cisplatin  
 20830-81-3, Daunorubicin 23214-92-8, Doxorubicin  
 33069-62-4, Taxol 41575-94-4, Carboplatin 95058-81-4,  
 Gemcitabine 97682-44-5, Irinotecan 113440-58-7,  
 Calicheamicin 114977-28-5, Docetaxel 152044-54-7,  
 Epothilone B 189453-10-9, Epothilone D  
 ROLE: THU (Therapeutic use); BIOL (Biological study); USES  
 (Uses)  
 (cancer therapy with **aptamers** and; stabilized  
**aptamers** to growth factors and their receptors  
 for use in treatment of solid tumors)

INDEX TERM: 808128-36-1 808197-55-9 808197-56-0 808197-57-1  
 808197-58-2 808197-59-3 808197-60-6 808197-61-7  
 808200-05-7 808200-06-8 808200-07-9 808200-08-0  
 808200-09-1 808200-10-4 808200-11-5 808200-12-6  
 808200-13-7 808200-14-8 808200-15-9 808200-16-0  
 808200-17-1 808200-18-2 808200-19-3 808200-20-6  
 808200-21-7 808200-22-8 808200-23-9 808200-24-0  
 808200-25-1 808200-26-2 808200-27-3 808200-28-4  
 808200-29-5 808200-30-8 808200-31-9 808200-32-0  
 808200-33-1 808200-34-2 808200-35-3 808200-36-4  
 808200-37-5 808200-38-6 808200-39-7 808200-40-0  
 808200-41-1 808793-77-3 808793-78-4 808793-79-5  
 808793-80-8 808793-81-9 808793-82-0 808793-83-1  
 808793-84-2 808793-85-3 808793-86-4 808793-87-5  
 808793-88-6 808793-89-7 808793-90-0 808793-91-1  
 808793-92-2 808793-93-3 808793-94-4 808793-95-5  
 808793-96-6 808793-97-7 808793-98-8 808793-99-9

808794-00-5 809292-29-3 809292-30-6  
 ROLE: BSU (Biological study, unclassified); PRP  
 (Properties); THU (Therapeutic use); BIOL (Biological  
 study); USES (Uses)  
 (nucleotide sequence, **aptamer** for  
 platelet-derived growth factor; stabilized  
**aptamers** to growth factors and their receptors  
 for use in treatment of solid tumors)  
 INDEX TERM: 120-73-0D, 1H-Purine, derivs.  
 ROLE: BSU (Biological study, unclassified); BIOL (Biological  
 study)  
 (purines, inhibitors of synthesis of, cancer therapy with  
**aptamers** and; stabilized **aptamers** to  
 growth factors and their receptors for use in treatment  
 of solid tumors)  
 INDEX TERM: 127464-60-2, Vascular endothelial growth factor  
 ROLE: BSU (Biological study, unclassified); BIOL (Biological  
 study)  
 (stabilized **aptamers** to growth factors and  
 their receptors for use in treatment of solid tumors)  
 INDEX TERM: 808200-49-9 808200-50-2 808200-51-3 808200-52-4  
 808200-53-5 808200-54-6 808200-55-7 808200-56-8  
 808200-57-9 808200-58-0  
 ROLE: PRP (Properties)  
 (unclaimed nucleotide sequence; stabilized  
**aptamers** to growth factors and their receptors  
 for use in the treatment of solid tumors)

L11 ANSWER 11 OF 17 CAPLUS COPYRIGHT 2005 ACS on STN  
 ACCESSION NUMBER: 2004:70006 CAPLUS  
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 ENTRY DATE: Entered STN: 28 Jan 2004  
 TITLE: Method of screening for **bivalent** binding  
 nucleic acid ligands (**aptamers**) of 7  
 transmembrane G protein-coupled receptors for  
 therapeutic and diagnostic use  
 INVENTOR(S): Gold, Larry  
 PATENT ASSIGNEE(S): Gilead Sciences, Inc., USA  
 SOURCE: U.S., 17 pp., Cont.-in-part of U.S. Ser. No. 956,699.  
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 MAIN: C12Q001-68  
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 536025400  
 CLASSIFICATION: 3-1 (Biochemical Genetics)  
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US 6682886	B1	20040127	US 1998-118525	19980717
US 5683867	A	19971104	US 1994-234997	19940428
US 6083696	A	20000704	US 1997-956699	19971023
WO 2000004184	A1	20000127	WO 1999-US14853	19990630
W:	AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM,			

TR, TT, UA, UG, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK,				
ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG,				
CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
AU 9947287	A1	20000207	AU 1999-47287	19990630
EP 1100960	A1	20010523	EP 1999-930840	19990630
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,				
IE, FI				
AU 773741	B2	20040603	AU 2001-18257	20010202
AU 773815	B2	20040610	AU 2001-29834	20010323
US 2004091931	A1	20040513	US 2003-729667	20031205
PRIORITY APPLN. INFO.:				
			US 1994-234997	A1 19940428
			US 1997-956699	A2 19971023
			US 1990-536428	B2 19900611
			AU 1991-82061	A0 19910610
			US 1991-714131	A2 19910610
			US 1993-117991	B2 19930908
			US 1993-123935	B2 19930917
			US 1994-199507	A2 19940222
			US 1994-234797	A2 19940428
			AU 1996-58839	A3 19960530
			AU 1996-61611	A3 19960604
			US 1998-118525	A 19980717
			WO 1999-US14853	W 19990630

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PATENT NO.	CLASS	PATENT FAMILY CLASSIFICATION CODES
US 6682886	ICM	C12Q001-68
	ICS	C12P019-34
	INCL	435006000; 435091200; 935077000; 935078000; 536023100; 536025400
US 6682886	NCL	435/006.000; 435/091.200; 536/023.100; 536/025.400
US 5683867	NCL	435/006.000; 435/091.200; 536/023.100; 536/025.400
	ECLA	C07H019/06E; C07H019/10E; C07H021/00C2; C07H021/00C4; C12N015/10C4; C12N015/11D; C12Q001/68A8+525/101; C12Q001/68A8; G01N033/532; G01N033/535; G01N033/68; G01N033/76
US 6083696	NCL	435/006.000; 435/091.200; 536/023.100; 536/024.300; 536/025.400
WO 2000004184	ECLA	C12Q001/68A8
US 2004091931	NCL	435/006.000; 435/007.100; 435/069.100; 435/320.100; 435/325.000; 530/350.000; 525/054.100; 530/395.000

ABSTRACT:

Methods for identifying and preparing **bivalent** binding mols. to 7 transmembrane domain containing G protein-coupled receptors, that can activate or inhibit 7 transmembrane G protein-coupled receptors, are described. SELEX (Systematic Evolution of Ligands by EXponential enrichment) method is used to screening high affinity nucleic acid ligands, also termed **aptamers**. It combines two or more binding domains to two or more different epitopes of the same 7 transmembrane G protein-coupled receptor. These SELEX-derived **\*\*\*bivalent\*\*\*** binding mols. comprise two or more binding domains which bind simultaneously to two or more epitopes of the same 7TM G protein-coupled receptor, thus has increased binding affinity to 7TM G protein-coupled receptor for their activation or inhibition. The method was exemplified by screening random RNA libraries for binding mols. to both ECL1 (extracellular loop 1) or ECL2 of neurokinin receptor NK1R using peptide affinity columns. The **\*\*\*bivalent\*\*\*** ligands, derived from two ECL1- and ECL1-binding RNA libraries by linking them through overlap-extension PCR reaction, can be enriched after cycles of SELEX process to generate double-stranded DNA templates for their future synthesis. These **bivalent** binding mols. may be useful as therapeutic and diagnostic agents.

SUPPL. TERM: drug screening **bivalent aptamer** 7TM G  
INDEX TERM: protein coupled receptor  
Neurotensin receptors  
ROLE: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)  
(A, of human, screening for **bivalent** nuclear acid ligands binding to peptides of; method of screening for **bivalent** binding **aptamers** of 7 transmembrane GPCRs for therapeutic and diagnostic use)

INDEX TERM: Parathyroid hormone receptors  
Secretin receptors  
ROLE: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)  
(A, of rat/opossum, screening for **bivalent** nuclear acid ligands binding to peptides of; method of screening for **bivalent** binding **aptamers** of 7 transmembrane GPCRs for therapeutic and diagnostic use)

INDEX TERM: Adenosine receptors  
ROLE: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)  
(A1, of rat or human or canine, screening for **bivalent** nuclear acid ligands binding to; method of screening for **bivalent** binding **aptamers** of 7 transmembrane GPCRs for therapeutic and diagnostic use)

INDEX TERM: Adenosine receptors  
ROLE: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)  
(A2B, of rat or human or sheep, screening for **bivalent** nuclear acid ligands binding to; method of screening for **bivalent** binding **aptamers** of 7 transmembrane GPCRs for therapeutic and diagnostic use)

INDEX TERM: Adenosine receptors  
ROLE: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)  
(A3, of human or sheep, screening for **bivalent** nuclear acid ligands binding to; method of screening for **bivalent** binding **aptamers** of 7 transmembrane GPCRs for therapeutic and diagnostic use)

INDEX TERM: Bradykinin receptors  
ROLE: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)  
(B2, of human/rat, screening for **bivalent** nuclear acid ligands binding to peptides of; method of screening for **bivalent** binding **aptamers** of 7 transmembrane GPCRs for therapeutic and diagnostic use)

INDEX TERM: Cholecystokinin receptors  
ROLE: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)  
(CCKA, of human/rat, screening for **bivalent** nuclear acid ligands binding to peptides of; method of screening for **bivalent** binding **aptamers** of 7 transmembrane GPCRs for therapeutic and diagnostic use)

INDEX TERM: Cholecystokinin receptors  
ROLE: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)  
(CCKB, of canine or human, screening for **bivalent** nuclear acid ligands binding to peptides of; method of

screening for **bivalent** binding **aptamers**  
of 7 transmembrane GPCRs for therapeutic and diagnostic  
use)

INDEX TERM: Dopamine receptors  
ROLE: BUU (Biological use, unclassified); BIOL (Biological  
study); USES (Uses)  
(D1, of rat or human or rhesus, screening for  
**bivalent** nuclear acid ligands binding to; method  
of screening for **bivalent** binding  
**aptamers** of 7 transmembrane GPCRs for therapeutic  
and diagnostic use)

INDEX TERM: Dopamine receptors  
ROLE: BUU (Biological use, unclassified); BIOL (Biological  
study); USES (Uses)  
(D1A, of rat or human or rhesus, screening for  
**bivalent** nuclear acid ligands binding to; method  
of screening for **bivalent** binding  
**aptamers** of 7 transmembrane GPCRs for therapeutic  
and diagnostic use)

INDEX TERM: Dopamine receptors  
ROLE: BUU (Biological use, unclassified); BIOL (Biological  
study); USES (Uses)  
(D2, of rat or human or mouse, screening for  
**bivalent** nuclear acid ligands binding to; method  
of screening for **bivalent** binding  
**aptamers** of 7 transmembrane GPCRs for therapeutic  
and diagnostic use)

INDEX TERM: Dopamine receptors  
ROLE: BUU (Biological use, unclassified); BIOL (Biological  
study); USES (Uses)  
(D3, of rat or human, screening for **bivalent**  
nuclear acid ligands binding to; method of screening for  
**bivalent** binding **aptamers** of 7  
transmembrane GPCRs for therapeutic and diagnostic use)

INDEX TERM: Dopamine receptors  
ROLE: BUU (Biological use, unclassified); BIOL (Biological  
study); USES (Uses)  
(D4, of human, screening for **bivalent** nuclear  
acid ligands binding to; method of screening for  
**bivalent** binding **aptamers** of 7  
transmembrane GPCRs for therapeutic and diagnostic use)

INDEX TERM: Dopamine receptors  
ROLE: BUU (Biological use, unclassified); BIOL (Biological  
study); USES (Uses)  
(D5, of rat or human, screening for **bivalent**  
nuclear acid ligands binding to; method of screening for  
**bivalent** binding **aptamers** of 7  
transmembrane GPCRs for therapeutic and diagnostic use)

INDEX TERM: 5-HT receptors  
ROLE: BUU (Biological use, unclassified); BIOL (Biological  
study); USES (Uses)  
(GP2-7 or 5A or 5A(S12) or 5B, of mouse/human, screening  
for **bivalent** nuclear acid ligands binding to  
peptides of; method of screening for **bivalent**  
binding **aptamers** of 7 transmembrane GPCRs for  
therapeutic and diagnostic use)

INDEX TERM: Histamine receptors  
ROLE: BUU (Biological use, unclassified); BIOL (Biological  
study); USES (Uses)  
(H1, of bovine, screening for **bivalent** nuclear  
acid ligands binding to; method of screening for  
**bivalent** binding **aptamers** of 7

INDEX TERM: transmembrane GPCRs for therapeutic and diagnostic use)  
Histamine receptors  
ROLE: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)  
(H2, of rat or canine or human, screening for  
**bivalent** nuclear acid ligands binding to; method  
of screening for **bivalent** binding  
**aptamers** of 7 transmembrane GPCRs for therapeutic  
and diagnostic use)

INDEX TERM: Muscarinic receptors  
ROLE: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)  
(M1, of mouse or human, screening for **bivalent**  
nuclear acid ligands binding to; method of screening for  
**bivalent** binding **aptamers** of 7  
transmembrane GPCRs for therapeutic and diagnostic use)

INDEX TERM: Muscarinic receptors  
ROLE: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)  
(M2, of human, screening for **bivalent** nuclear  
acid ligands binding to; method of screening for  
**bivalent** binding **aptamers** of 7  
transmembrane GPCRs for therapeutic and diagnostic use)

INDEX TERM: Muscarinic receptors  
ROLE: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)  
(M3, of human, screening for **bivalent** nuclear  
acid ligands binding to; method of screening for  
**bivalent** binding **aptamers** of 7  
transmembrane GPCRs for therapeutic and diagnostic use)

INDEX TERM: Muscarinic receptors  
ROLE: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)  
(M4, of human or chicken, screening for **bivalent**  
nuclear acid ligands binding to; method of screening for  
**bivalent** binding **aptamers** of 7  
transmembrane GPCRs for therapeutic and diagnostic use)

INDEX TERM: Muscarinic receptors  
ROLE: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)  
(M5, of human/rat, screening for **bivalent**  
nuclear acid ligands binding to; method of screening for  
**bivalent** binding **aptamers** of 7  
transmembrane GPCRs for therapeutic and diagnostic use)

INDEX TERM: Oligonucleotides  
ROLE: BSU (Biological study, unclassified); PUR  
(Purification or recovery); SPN (Synthetic preparation);  
BIOL (Biological study); PREP (Preparation)  
(RNA **aptamers**, binding to G protein  
coupled-receptor epitopes; method of screening for  
**bivalent** binding **aptamers** of 7  
transmembrane GPCRs for therapeutic and diagnostic use)

INDEX TERM: Genetic methods  
(SELEX; method of screening for **bivalent**  
binding **aptamers** of 7 transmembrane GPCRs for  
therapeutic and diagnostic use)

INDEX TERM: Somatostatin receptors  
ROLE: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)  
(SSTR1, of rat/human, screening for **bivalent**  
nuclear acid ligands binding to peptides of; method of  
screening for **bivalent** binding **aptamers**

of 7 transmembrane GPCRs for therapeutic and diagnostic use)

INDEX TERM: Somatostatin receptors  
ROLE: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)  
(SSTR2, of mouse, screening for **bivalent** nuclear acid ligands binding to peptides of; method of screening for **bivalent** binding **aptamers** of 7 transmembrane GPCRs for therapeutic and diagnostic use)

INDEX TERM: Somatostatin receptors  
ROLE: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)  
(SSTR3, of rat/human/mouse, screening for **bivalent** nuclear acid ligands binding to peptides of; method of screening for **bivalent** binding **aptamers** of 7 transmembrane GPCRs for therapeutic and diagnostic use)

INDEX TERM: Somatostatin receptors  
ROLE: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)  
(SSTR4, of human/mouse, screening for **bivalent** nuclear acid ligands binding to peptides of; method of screening for **bivalent** binding **aptamers** of 7 transmembrane GPCRs for therapeutic and diagnostic use)

INDEX TERM: Somatostatin receptors  
ROLE: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)  
(SSTR5, of human/mouse, screening for **bivalent** nuclear acid ligands binding to peptides of; method of screening for **bivalent** binding **aptamers** of 7 transmembrane GPCRs for therapeutic and diagnostic use)

INDEX TERM: Polysiloxanes, biological studies  
ROLE: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)  
(amino, **aptamers** linked by; method of screening for **bivalent** binding **aptamers** of 7 transmembrane GPCRs for therapeutic and diagnostic use)

INDEX TERM: Angiotensin receptors  
ROLE: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)  
(angiotensin II, of human/rat/mouse, screening for **bivalent** nuclear acid ligands binding to peptides of; method of screening for **bivalent** binding **aptamers** of 7 transmembrane GPCRs for therapeutic and diagnostic use)

INDEX TERM: Liposomes  
(**aptamers** linked by; method of screening for **bivalent** binding **aptamers** of 7 transmembrane GPCRs for therapeutic and diagnostic use)

INDEX TERM: Hydrocarbons, biological studies  
Monosaccharides  
Oligosaccharides, biological studies  
Peptides, biological studies  
Polynucleotides  
Polyoxyalkylenes, biological studies  
Proteins  
ROLE: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)  
(**aptamers** linked by; method of screening for

INDEX TERM: **bivalent binding aptamers** of 7  
transmembrane GPCRs for therapeutic and diagnostic use)  
INDEX TERM: **Polysiloxanes**, biological studies  
ROLE: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)  
(hydroxy, **aptamers** linked by; method of screening for **bivalent binding aptamers** of 7 transmembrane GPCRs for therapeutic and diagnostic use)  
INDEX TERM: **DNA**  
ROLE: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)  
(linker, for generation of **bivalent** RNA ligands to G protein-coupled receptors epitopes; method of screening for **bivalent binding aptamers** of 7 transmembrane GPCRs for therapeutic and diagnostic use)  
INDEX TERM: **Canis familiaris**  
Human  
Mus  
**Rattus**  
(method of screening for **bivalent** binding **aptamers** of 7 transmembrane GPCRs for therapeutic and diagnostic use)  
INDEX TERM: **G protein-coupled receptors**  
ROLE: BSU (Biological study, unclassified); BIOL (Biological study)  
(method of screening for **bivalent** binding **aptamers** of 7 transmembrane GPCRs for therapeutic and diagnostic use)  
INDEX TERM: **Epitopes**  
(of G protein-coupled receptors; method of screening for **bivalent binding aptamers** of 7 transmembrane GPCRs for therapeutic and diagnostic use)  
INDEX TERM: **Thyrotropin receptors**  
ROLE: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)  
(of canine/rat or human, screening for **bivalent** nuclear acid ligands binding to peptides of; method of screening for **bivalent binding aptamers** of 7 transmembrane GPCRs for therapeutic and diagnostic use)  
INDEX TERM: **Gonadotropin-releasing hormone receptor**  
**VIP receptors**  
ROLE: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)  
(of human, screening for **bivalent** nuclear acid ligands binding to peptides of; method of screening for **bivalent binding aptamers** of 7 transmembrane GPCRs for therapeutic and diagnostic use)  
INDEX TERM: **Gonadotropin receptors**  
ROLE: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)  
(of human/rat/mouse, screening for **bivalent** nuclear acid ligands binding to peptides of; method of screening for **bivalent binding aptamers** of 7 transmembrane GPCRs for therapeutic and diagnostic use)  
INDEX TERM: **Calcitonin receptors**  
ROLE: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)  
(of human/rat/pig, screening for **bivalent**

INDEX TERM: nuclear acid ligands binding to peptides of; method of screening for **bivalent binding aptamers** of 7 transmembrane GPCRs for therapeutic and diagnostic use)

INDEX TERM: Corticotropin releasing factor receptors

Glucagon receptors

Growth hormone-releasing hormone receptors

Neuropeptide Y receptors

ROLE: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)

(of rat, screening for **bivalent** nuclear acid ligands binding to peptides of; method of screening for **bivalent binding aptamers** of 7 transmembrane GPCRs for therapeutic and diagnostic use)

INDEX TERM: Muscarinic receptors

ROLE: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)

(of swine or Drosophila, screening for **bivalent** nuclear acid ligands binding to; method of screening for **bivalent binding aptamers** of 7 transmembrane GPCRs for therapeutic and diagnostic use)

INDEX TERM: Affinity chromatography

(screening for **bivalent** ligand to G protein-coupled receptors epitopes; method of screening for **bivalent binding aptamers** of 7 transmembrane GPCRs for therapeutic and diagnostic use)

INDEX TERM: Polysiloxanes, biological studies

ROLE: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)

(thio or carboxy-functionalized, **aptamers** linked by; method of screening for **bivalent binding aptamers** of 7 transmembrane GPCRs for therapeutic and diagnostic use)

INDEX TERM: PCR (polymerase chain reaction)

(to link G protein coupled receptor epitope ECL1- or ECL2-binding RNA mols.; method of screening for **bivalent binding aptamers** of 7 transmembrane GPCRs for therapeutic and diagnostic use)

INDEX TERM: 5-HT receptors

ROLE: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)

(type 5-HT1, 1C, of mouse/human, screening for **bivalent** nuclear acid ligands binding to peptides of; method of screening for **bivalent binding aptamers** of 7 transmembrane GPCRs for therapeutic and diagnostic use)

INDEX TERM: 5-HT receptors

ROLE: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)

(type 5-HT1, of rat, screening for **bivalent** nuclear acid ligands binding to peptides of; method of screening for **bivalent binding aptamers** of 7 transmembrane GPCRs for therapeutic and diagnostic use)

INDEX TERM: 5-HT receptors

ROLE: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)

(type 5-HT1A, of rat/human, screening for **bivalent** nuclear acid ligands binding to peptides of; method of screening for **bivalent binding aptamers** of 7 transmembrane GPCRs for therapeutic and diagnostic use)

INDEX TERM: 5-HT receptors  
ROLE: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)  
(type 5-HT1B, of rat/human/mouse, screening for **bivalent** nuclear acid ligands binding to peptides of; method of screening for **bivalent** binding **aptamers** of 7 transmembrane GPCRs for therapeutic and diagnostic use)

INDEX TERM: 5-HT receptors  
ROLE: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)  
(type 5-HT1D, of canine/human, screening for **bivalent** nuclear acid ligands binding to peptides of; method of screening for **bivalent** binding **aptamers** of 7 transmembrane GPCRs for therapeutic and diagnostic use)

INDEX TERM: 5-HT receptors  
ROLE: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)  
(type 5-HT1E, of rat, screening for **bivalent** nuclear acid ligands binding to peptides of; method of screening for **bivalent** binding **aptamers** of 7 transmembrane GPCRs for therapeutic and diagnostic use)

INDEX TERM: 5-HT receptors  
ROLE: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)  
(type 5-HT2, of rat, screening for **bivalent** nuclear acid ligands binding to peptides of; method of screening for **bivalent** binding **aptamers** of 7 transmembrane GPCRs for therapeutic and diagnostic use)

INDEX TERM: 5-HT receptors  
ROLE: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)  
(type 5-HT2B, of human, screening for **bivalent** nuclear acid ligands binding to peptides of; method of screening for **bivalent** binding **aptamers** of 7 transmembrane GPCRs for therapeutic and diagnostic use)

INDEX TERM: 5-HT receptors  
ROLE: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)  
(type 5-HT3, of mouse, screening for **bivalent** nuclear acid ligands binding to peptides of; method of screening for **bivalent** binding **aptamers** of 7 transmembrane GPCRs for therapeutic and diagnostic use)

INDEX TERM: 5-HT receptors  
ROLE: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)  
(type 5-HT7, of rat, screening for **bivalent** nuclear acid ligands binding to peptides of; method of screening for **bivalent** binding **aptamers** of 7 transmembrane GPCRs for therapeutic and diagnostic use)

INDEX TERM: Endothelin receptors  
ROLE: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)  
(type ETB, of human, screening for **bivalent** nuclear acid ligands binding to peptides of; method of screening for **bivalent** binding **aptamers**)

of 7 transmembrane GPCRs for therapeutic and diagnostic use)

INDEX TERM: Tachykinin receptors  
ROLE: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)  
(type NK1, of human/mouse/rat, screening for **bivalent** nuclear acid ligands binding to peptides of; method of screening for **bivalent** binding **aptamers** of 7 transmembrane GPCRs for therapeutic and diagnostic use)

INDEX TERM: Opioid receptors  
ROLE: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)  
( $\kappa$ -opioid, of human/rat/mouse, screening for **bivalent** nuclear acid ligands binding to; method of screening for **bivalent** binding **aptamers** of 7 transmembrane GPCRs for therapeutic and diagnostic use)

INDEX TERM: Adrenoceptors  
ROLE: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)  
( $\alpha$ 1, of hamster or bovine, screening for **bivalent** nuclear acid ligands binding to; method of screening for **bivalent** binding **aptamers** of 7 transmembrane GPCRs for therapeutic and diagnostic use)

INDEX TERM: Adrenoceptors  
ROLE: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)  
( $\alpha$ 1D, of rat, screening for **bivalent** nuclear acid ligands binding to; method of screening for **bivalent** binding **aptamers** of 7 transmembrane GPCRs for therapeutic and diagnostic use)

INDEX TERM: Adrenoceptors  
ROLE: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)  
( $\alpha$ 2, of human or mouse or fish, screening for **bivalent** nuclear acid ligands binding to; method of screening for **bivalent** binding **aptamers** of 7 transmembrane GPCRs for therapeutic and diagnostic use)

INDEX TERM: Adrenoceptors  
ROLE: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)  
( $\alpha$ 2, of human or rat, screening for **bivalent** nuclear acid ligands binding to; method of screening for **bivalent** binding **aptamers** of 7 transmembrane GPCRs for therapeutic and diagnostic use)

INDEX TERM: Adrenoceptors  
ROLE: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)  
( $\alpha$ 2A, of human or porcine or rat, screening for **bivalent** nuclear acid ligands binding to; method of screening for **bivalent** binding **aptamers** of 7 transmembrane GPCRs for therapeutic and diagnostic use)

INDEX TERM: Adrenoceptors  
ROLE: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)  
( $\alpha$ 2B, of human or rat, screening for **bivalent** nuclear acid ligands binding to; method

INDEX TERM: Adrenoceptors  
ROLE: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)  
( $\alpha$ 2C, of mouse or rat, screening for bivalent nuclear acid ligands binding to; method of screening for bivalent binding aptamers of 7 transmembrane GPCRs for therapeutic and diagnostic use)

INDEX TERM: Adrenoceptors  
ROLE: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)  
( $\beta$ 1, of rat or human or mouse, screening for bivalent nuclear acid ligands binding to; method of screening for bivalent binding aptamers of 7 transmembrane GPCRs for therapeutic and diagnostic use)

INDEX TERM: Adrenoceptors  
ROLE: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)  
( $\beta$ 2, of rat or human or mouse, screening for bivalent nuclear acid ligands binding to; method of screening for bivalent binding aptamers of 7 transmembrane GPCRs for therapeutic and diagnostic use)

INDEX TERM: Adrenoceptors  
ROLE: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)  
( $\beta$ 3, of rat or human or bovine, screening for bivalent nuclear acid ligands binding to; method of screening for bivalent binding aptamers of 7 transmembrane GPCRs for therapeutic and diagnostic use)

INDEX TERM: Opioid receptors  
ROLE: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)  
( $\delta$ -opioid, of human/mouse, screening for bivalent nuclear acid ligands binding to; method of screening for bivalent binding aptamers of 7 transmembrane GPCRs for therapeutic and diagnostic use)

INDEX TERM: Opioid receptors  
ROLE: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)  
( $\mu$ -opioid, of human/rat, screening for bivalent nuclear acid ligands binding to; method of screening for bivalent binding aptamers of 7 transmembrane GPCRs for therapeutic and diagnostic use)

INDEX TERM: 9002-89-5, Ethenol, homopolymer 9003-01-4, 2-Propenoic acid homopolymer 9004-53-9, Dextrin 12619-70-4, Cyclodextrin 25322-68-3, Poly(oxy-1,2-ethanediyl),  $\alpha$ -hydro- $\omega$ -hydroxy- 25322-69-4, Poly[oxy(methyl-1,2-ethanediyl)],  $\alpha$ -hydro- $\omega$ -hydroxy-  
ROLE: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)  
(aptamers linked by; method of screening for bivalent binding aptamers of 7 transmembrane GPCRs for therapeutic and diagnostic use)

INDEX TERM: 268720-50-9P, RNA (synthetic)  
ROLE: BPN (Biosynthetic preparation); BSU (Biological study, unclassified); PUR (Purification or recovery); BIOL (Biological study); PREP (Preparation)  
(as ligands to G protein coupled-receptor; method of screening for **bivalent binding aptamers** of 7 transmembrane GPCRs for therapeutic and diagnostic use)

INDEX TERM: 255916-21-3, L-Phenylalanine, L-histidyl-L-asparaginyl-L- $\alpha$ -glutamyl-L-tryptophyl-L-tyrosyl-L-tyrosylglycyl-L-leucyl-L-phenylalanyl-L-tyrosyl-L-cysteinyl-L-lysyl-  
ROLE: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)  
(neurokinin receptor 1 extracellular loop 1; method of screening for **bivalent binding aptamers** of 7 transmembrane GPCRs for therapeutic and diagnostic use)

INDEX TERM: 255916-22-4, L-Valine, L-threonyl-L-threonyl-L- $\alpha$ -glutamyl-L-threonyl-L-methionyl-L-proyl-L-seryl-L-arginyl-L-valyl-L-valyl-L-cysteinyl-L-methionyl-L-isoleucyl-L- $\alpha$ -glutamyl-L-tryptophyl-L-proyl-L- $\alpha$ -glutamyl-L-histidyl-L-proyl-L-asparaginyl-L-lysyl-L-isoleucyl-L-tyrosyl-L- $\alpha$ -glutamyl-L-lysyl-  
ROLE: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)  
(neurokinin receptor 1 extracellular loop 2; method of screening for **bivalent binding aptamers** of 7 transmembrane GPCRs for therapeutic and diagnostic use)

REFERENCE COUNT: 29 THERE ARE 29 CITED REFERENCES AVAILABLE FOR THIS RECORD.

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(2) Anon; WO 8906694 1989 CAPLUS  
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L11 ANSWER 12 OF 17 CAPLUS COPYRIGHT 2005 ACS on STN  
ACCESSION NUMBER: 2003:290966 CAPLUS  
DOCUMENT NUMBER: 139:18071  
ENTRY DATE: Entered STN: 16 Apr 2003  
TITLE: Yeast genetic selections to optimize RNA decoys for transcription factor NF- $\kappa$ B  
AUTHOR(S): Cassidy, Laura A.; Maher, L. James, III  
CORPORATE SOURCE: Department of Biochemistry and Molecular Biology, Mayo Foundation, Rochester, MN, 55905, USA  
SOURCE: Proceedings of the National Academy of Sciences of the United States of America (2003), 100(7), 3930-3935  
CODEN: PNASA6; ISSN: 0027-8424  
PUBLISHER: National Academy of Sciences  
DOCUMENT TYPE: Journal  
LANGUAGE: English  
CLASSIFICATION: 3-2 (Biochemical Genetics)  
Section cross-reference(s): 6

**ABSTRACT:**  
In vitro-selected RNA **aptamers** are potential inhibitors of disease-related proteins. The laboratory previously isolated an RNA **aptamer** that binds with high affinity to human transcription factor NF- $\kappa$ B. This RNA **aptamer** competitively inhibits DNA binding by NF- $\kappa$ B in vitro and is recognized by its target protein in vivo in a yeast three-hybrid system. In the present study, yeast genetic selections were used to optimize the RNA **aptamer** for binding to NF- $\kappa$ B in the eukaryotic nucleus. Selection for improved binding to NF- $\kappa$ B from RNA libraries encoding (i) degenerate **aptamer** variants and (ii) sequences present at round 8 of 14 total rounds of in vitro selection yielded RNA **aptamers** with dramatically improved in vivo activity. Furthermore, the authors show that an in vivo-optimized RNA **aptamer** exhibits specific "decoy" activity, inhibiting transcriptional activation by its NF- $\kappa$ B target protein in a yeast one-hybrid assay. This decoy activity is enhanced by the expression of a \*\*\*bivalent\*\*\* **aptamer**. The combination of in vitro and in vivo genetic selections was crucial for obtaining RNA **aptamers** with in vivo decoy activity.

SUPPL. TERM: RNA **aptamer** transcription factor NF $\kappa$ B yeast selection  
INDEX TERM: Transcription factors  
ROLE: BSU (Biological study, unclassified); BIOL (Biological study)  
(NF- $\kappa$ B (nuclear factor of  $\kappa$  light chain gene enhancer in B-cells); yeast three hybrid system to optimize  $\alpha$ -p50 RNA **aptamer** binding to human transcription factor NF- $\kappa$ B)  
INDEX TERM: **Aptamers**  
Combinatorial library  
(RNA; yeast three hybrid system to optimize  $\alpha$ -p50 RNA **aptamer** binding to human transcription factor NF- $\kappa$ B)  
INDEX TERM: Post-transcriptional processing  
(interference; yeast three hybrid system to optimize  $\alpha$ -p50 RNA **aptamer** binding to human transcription factor NF- $\kappa$ B)  
INDEX TERM: Genetic selection  
Human  
Molecular association  
Yeast  
(yeast three hybrid system to optimize  $\alpha$ -p50 RNA **aptamer** binding to human transcription factor NF- $\kappa$ B)

INDEX TERM: 539023-00-2 539023-01-3 539023-02-4 539023-03-5  
539023-04-6 539023-05-7 539023-06-8  
ROLE: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)  
(RNA **aptamer**; yeast three hybrid system to optimize  $\alpha$ -p50 RNA **aptamer** binding to human transcription factor NF- $\kappa$ B)

INDEX TERM: 539023-07-9  
ROLE: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)  
(yeast three hybrid system to optimize  $\alpha$ -p50 RNA **aptamer** binding to human transcription factor NF- $\kappa$ B)

REFERENCE COUNT: 25 THERE ARE 25 CITED REFERENCES AVAILABLE FOR THIS RECORD.

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L11 ANSWER 13 OF 17 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2002:595004 CAPLUS

DOCUMENT NUMBER: 137:151578

ENTRY DATE: Entered STN: 09 Aug 2002

TITLE: High affinity nucleic acid **aptamers**

incorporated into bi-specific capture ligands

Tahiri-Alaoui, Abdessamad; James, William S.

INVENTOR(S): Isis Innovation Limited, UK

PATENT ASSIGNEE(S): PCT Int. Appl., 41 pp.

SOURCE: CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

INT. PATENT CLASSIF.:

MAIN: C12N015-11

SECONDARY: C07H021-00; C12Q001-68

CLASSIFICATION: 6-2 (General Biochemistry)

FAMILY ACC. NUM. COUNT: 3

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002061079	A2	20020808	WO 2002-GB364	20020129
WO 2002061079	A3	20030904		
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW			
RW:	GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG			
PRIORITY APPLN. INFO.:			GB 2001-2270	A 20010129
			GB 2001-2271	A 20010129
			GB 2001-2272	A 20010129
			GB 2001-2273	A 20010129

PATENT CLASSIFICATION CODES:

PATENT NO.	CLASS	PATENT FAMILY CLASSIFICATION CODES
WO 2002061079	ICM	C12N015-11
	ICS	C07H021-00; C12Q001-68

ABSTRACT:

The present invention provides biligands which comprise at least two \*\*\*aptamers.\*\*\* In particular, a system for binding two **aptamers** together to provide **bivalent** or bispecific ligands is provided. The authors have isolated 2'-Fluoro-substituted RNA **aptamers** that bind to streptavidin (SA) with an affinity around  $7 \pm 1.8$  nM, comparable with that of recently described peptide **aptamers**. Binding to SA was not prevented by prior saturation with biotin, enabling nucleic acid **aptamers** to form useful ternary complexes. Mutagenesis, secondary structure anal., RNase footprinting and deletion anal. provided evidence for the essential structural features of SA-binding **aptamers**. In order to provide a general method for the exploitation of these **aptamers**, the authors produced derivs. in which they were fused to the naturally structured RNA elements, CopT or CopA. In parallel, the authors produced derivs. of CD4-binding **aptamers** fused to the complementary CopA or CopT elements. When mixed, these two chimeric **aptamers** rapidly hybridized, by virtue of CopA-CopT complementarity, to form stable, bi-functional **aptamers** that the authors called "adaptamers". The authors show that a CD4-SA-binding adaptamer can be used to capture CD4 onto a SA-derivatized surface, illustrating their general utility as indirect affinity ligands.

SUPPL. TERM: RNA streptavidin **aptamer** CD4 antigen CopA CopT fusion ligand

INDEX TERM: RNA  
ROLE: BSU (Biological study, unclassified); DGN (Diagnostic use); PRP (Properties); BIOL (Biological study); USES (Uses)  
(2'-Fluoro-substituted, as **aptamers**; high affinity nucleic acid **aptamers** incorporated into bi-specific capture ligands)

INDEX TERM: Nucleic acids  
ROLE: BSU (Biological study, unclassified); DGN (Diagnostic use); PRP (Properties); BIOL (Biological study); USES (Uses)  
(analogs, 2'-Fluoro-substituted, as **aptamers**; high affinity nucleic acid **aptamers** incorporated into bi-specific capture ligands)

INDEX TERM: CD4 (antigen)  
ROLE: BSU (Biological study, unclassified); BIOL (Biological

study)  
(aptamer binding to; high affinity nucleic acid  
aptamers incorporated into bi-specific capture  
ligands)

INDEX TERM: Plasmids  
(copA and copT, use in aptamers; high affinity  
nucleic acid aptamers incorporated into  
bi-specific capture ligands)

INDEX TERM: Gene, microbial  
ROLE: BUU (Biological use, unclassified); BIOL (Biological  
study); USES (Uses)  
(copA, use in aptamers; high affinity nucleic  
acid aptamers incorporated into bi-specific  
capture ligands)

INDEX TERM: Gene, microbial  
ROLE: BUU (Biological use, unclassified); BIOL (Biological  
study); USES (Uses)  
(copT, use in aptamers; high affinity nucleic  
acid aptamers incorporated into bi-specific  
capture ligands)

INDEX TERM: Envelope proteins  
ROLE: BSU (Biological study, unclassified); BIOL (Biological  
study)  
(gp120env, aptamer binding to; high affinity  
nucleic acid aptamers incorporated into  
bi-specific capture ligands)

INDEX TERM: rRNA sequences  
(high affinity nucleic acid aptamers  
incorporated into bi-specific capture ligands)

INDEX TERM: Ligands  
Nucleic acids  
ROLE: BSU (Biological study, unclassified); DGN (Diagnostic  
use); PRP (Properties); BIOL (Biological study); USES (Uses)  
(high affinity nucleic acid aptamers  
incorporated into bi-specific capture ligands)

INDEX TERM: 9013-20-1, Streptavidin  
ROLE: BSU (Biological study, unclassified); BIOL (Biological  
study)  
(aptamer binding to; high affinity nucleic acid  
aptamers incorporated into bi-specific capture  
ligands)

INDEX TERM: 445359-28-4, RNA (synthetic RNA aptamer J58copA)  
445359-29-5, RNA (synthetic RNA aptamer L45copT)  
ROLE: BSU (Biological study, unclassified); DGN (Diagnostic  
use); PRP (Properties); BIOL (Biological study); USES (Uses)  
(nucleotide sequence; high affinity nucleic acid  
aptamers incorporated into bi-specific capture  
ligands)

INDEX TERM: 445361-54-6 445361-55-7 445361-56-8 445361-57-9  
445361-58-0 445361-59-1 445361-60-4 445361-61-5  
ROLE: PRP (Properties)  
(unclaimed sequence; high affinity nucleic acid  
aptamers incorporated into bi-specific capture  
ligands)

L11 ANSWER 14 OF 17 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2002:200806 CAPLUS

DOCUMENT NUMBER: 136:336715

ENTRY DATE: Entered STN: 19 Mar 2002

TITLE: Forced engagement of a RNA/protein complex by a  
chemical inducer of dimerization to modulate gene  
expression

AUTHOR(S): Harvey, Isabelle; Garneau, Philippe; Pelletier, Jerry  
CORPORATE SOURCE: Department of Biochemistry, McGill University,  
Montreal, QC, H3G 1Y6, Can.  
SOURCE: Proceedings of the National Academy of Sciences of the  
United States of America (2002), 99(4), 1882-1887  
CODEN: PNASA6; ISSN: 0027-8424  
PUBLISHER: National Academy of Sciences  
DOCUMENT TYPE: Journal  
LANGUAGE: English  
CLASSIFICATION: 6-1 (General Biochemistry)  
ABSTRACT:  
A general strategy is described for forcing the engagement of an RNA/protein complex by using small-mol. ligands. A **bivalent** mol. was created by linking a protein-binding ligand to an RNA-binding ligand. On presentation of the chemical inducer of dimerization to the RNA by the protein, cooperative binding ensued, resulting in higher-affinity complexes. When the chemical inducer of dimerization was used to target the protein to an mRNA template, the resulting RNA/protein complex was sufficiently stable to inhibit mRNA translation. This approach provides a logic to modulate gene expression by using small-mol. ligands to recruit protein surfaces to mRNAs.  
SUPPL. TERM: translation inhibition artificial RNA protein complex  
INDEX TERM: Ribosome  
(80 S; inhibition of initiation complex formation by a forced engagement of a RNA/protein complex streptavidin)  
INDEX TERM: RNA  
ROLE: BSU (Biological study, unclassified); BIOL (Biological study)  
(aptamers J6f1, XI; translation inhibition by an artificial RNA-protein complex)  
INDEX TERM: Molecular association  
Translation initiation  
(translation inhibition by an artificial RNA-protein complex)  
INDEX TERM: 9013-20-1, Streptavidin  
ROLE: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)  
(inhibition of initiation complex formation by a forced engagement of a RNA/protein complex streptavidin)  
INDEX TERM: 419573-18-5 419573-19-6 419573-20-9  
ROLE: BSU (Biological study, unclassified); BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)  
(translation inhibition by an artificial RNA-protein complex)  
INDEX TERM: 58-85-5D, Biotin, derivs. 32986-56-4D, Tobramycin, derivs.  
ROLE: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)  
(translation inhibition by an artificial RNA-protein complex)  
REFERENCE COUNT: 32 THERE ARE 32 CITED REFERENCES AVAILABLE FOR THIS RECORD.  
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L11 ANSWER 15 OF 17 CAPLUS COPYRIGHT 2005 ACS on STN  
 ACCESSION NUMBER: 2000:68592 CAPLUS  
 DOCUMENT NUMBER: 132:105019  
 ENTRY DATE: Entered STN: 28 Jan 2000  
 TITLE: Synthesis and identification of **bivalent** binding RNA molecules to G protein-coupled receptors  
 INVENTOR(S): Gold, Larry  
 PATENT ASSIGNEE(S): Nexstar Pharmaceuticals, Inc., USA  
 SOURCE: PCT Int. Appl., 49 pp.  
 CODEN: PIXXD2  
 DOCUMENT TYPE: Patent  
 LANGUAGE: English  
 INT. PATENT CLASSIF.:  
 MAIN: C12Q001-68  
 SECONDARY: C12P019-34  
 CLASSIFICATION: 9-14 (Biochemical Methods)  
 Section cross-reference(s): 1, 2, 3  
 FAMILY ACC. NUM. COUNT: 127  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000004184	A1	20000127	WO 1999-US14853	19990630
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
US 6682886	B1	20040127	US 1998-118525	19980717
AU 9947287	A1	20000207	AU 1999-47287	19990630
EP 1100960	A1	20010523	EP 1999-930840	19990630
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,				

IE, FI				
AU 773741	B2	20040603	AU 2001-18257	20010202
AU 773815	B2	20040610	AU 2001-29834	20010323
PRIORITY APPLN. INFO.:				
			US 1998-118525	A 19980717
			AU 1991-82061	A0 19910610
			US 1994-234997	A1 19940428
			AU 1996-58839	A3 19960530
			AU 1996-61611	A3 19960604
			US 1997-956699	A2 19971023
			WO 1999-US14853	W 19990630

PATENT CLASSIFICATION CODES:

PATENT NO.	CLASS	PATENT FAMILY CLASSIFICATION CODES
WO 2000004184	ICM	C12Q001-68
	ICS	C12P019-34
WO 2000004184	ECLA	C12Q001/68A8
US 6682886	NCL	435/006.000; 435/091.200; 536/023.100; 536/025.400

ABSTRACT:

Methods for identifying and preparing **bivalent** binding mols. to 7 transmembrane domain containing G protein-coupled receptors are described. The methods are based on the SELEX method (Systematic Evolution of Ligands by EXponential enrichment) for generating high affinity nucleic acid ligands, termed **aptamers**. It combines two or more binding domains to two or more different epitopes of the same 7 transmembrane G protein-coupled receptor. The method was exemplified by screening in the random RNA library for binding mols. to either ECL1 (extracellular loop 1) or ECL2 of neurokinin receptor NK1R using peptide affinity columns. The **bivalent** ligands, derived from two ECL1- and ECL1-binding RNA libraries by linking them through overlap-extension PCR reaction, can be enriched after cycles of SELEX process to generate double-stranded DNA templates for their future synthesis. These \*\*\*bivalent\*\*\* binding mols. may be useful as therapeutic and diagnostic agents.

SUPPL. TERM: biosynthesis screening **bivalent** binding mol G  
 protein coupled receptor; **aptamers**  
**bivalent** substance P receptor NK1R SELEX

INDEX TERM: 5-HT receptors  
 ROLE: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)  
 (5-HT1, 1C, of mouse/human, screening for  
**bivalent** nuclear acid ligands binding to peptides  
 of; synthesis and identification of **bivalent**  
 binding RNA mols. to G protein-coupled receptors)

INDEX TERM: 5-HT receptors  
 ROLE: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)  
 (5-HT1, of rat, screening for **bivalent** nuclear  
 acid ligands binding to peptides of; synthesis and  
 identification of **bivalent** binding RNA mols. to  
 G protein-coupled receptors)

INDEX TERM: 5-HT receptors  
 ROLE: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)  
 (5-HT1A, of rat/human, screening for **bivalent**  
 nuclear acid ligands binding to peptides of; synthesis  
 and identification of **bivalent** binding RNA  
 mols. to G protein-coupled receptors)

INDEX TERM: 5-HT receptors  
 ROLE: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)  
 (5-HT1B, of rat/human/mouse, screening for  
**bivalent** nuclear acid ligands binding to peptides

INDEX TERM: 5-HT receptors  
ROLE: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)  
(5-HT1D, of canine/human, screening for **bivalent** nuclear acid ligands binding to peptides of; synthesis and identification of **bivalent** binding RNA mols. to G protein-coupled receptors)

INDEX TERM: 5-HT receptors  
ROLE: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)  
(5-HT1E, of rat, screening for **bivalent** nuclear acid ligands binding to peptides of; synthesis and identification of **bivalent** binding RNA mols. to G protein-coupled receptors)

INDEX TERM: 5-HT receptors  
ROLE: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)  
(5-HT2, of rat, screening for **bivalent** nuclear acid ligands binding to peptides of; synthesis and identification of **bivalent** binding RNA mols. to G protein-coupled receptors)

INDEX TERM: 5-HT receptors  
ROLE: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)  
(5-HT2B, of human, screening for **bivalent** nuclear acid ligands binding to peptides of; synthesis and identification of **bivalent** binding RNA mols. to G protein-coupled receptors)

INDEX TERM: 5-HT receptors  
ROLE: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)  
(5-HT3, of mouse, screening for **bivalent** nuclear acid ligands binding to peptides of; synthesis and identification of **bivalent** binding RNA mols. to G protein-coupled receptors)

INDEX TERM: 5-HT receptors  
ROLE: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)  
(5-HT7, of rat, screening for **bivalent** nuclear acid ligands binding to peptides of; synthesis and identification of **bivalent** binding RNA mols. to G protein-coupled receptors)

INDEX TERM: Neurotensin receptors  
ROLE: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)  
(A, of human, screening for **bivalent** nuclear acid ligands binding to peptides of; synthesis and identification of **bivalent** binding RNA mols. to G protein-coupled receptors)

INDEX TERM: Parathyroid hormone receptors  
Secretin receptors  
ROLE: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)  
(A, of rat/possum, screening for **bivalent** nuclear acid ligands binding to peptides of; synthesis and identification of **bivalent** binding RNA mols. to G protein-coupled receptors)

INDEX TERM: Adenosine receptors  
ROLE: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)

INDEX TERM: Adenosine receptors  
ROLE: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)  
(A1, of rat or human or canine, screening for **bivalent** nuclear acid ligands binding to; synthesis and identification of **bivalent** binding RNA mols. to G protein-coupled receptors)

INDEX TERM: Adenosine receptors  
ROLE: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)  
(A2B, of rat or human or sheep, screening for **bivalent** nuclear acid ligands binding to; synthesis and identification of **bivalent** binding RNA mols. to G protein-coupled receptors)

INDEX TERM: Adenosine receptors  
ROLE: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)  
(A3, of human or sheep, screening for **bivalent** nuclear acid ligands binding to; synthesis and identification of **bivalent** binding RNA mols. to G protein-coupled receptors)

INDEX TERM: Bradykinin receptors  
ROLE: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)  
(B2, of human/rat, screening for **bivalent** nuclear acid ligands binding to peptides of; synthesis and identification of **bivalent** binding RNA mols. to G protein-coupled receptors)

INDEX TERM: Dopamine receptors  
ROLE: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)  
(D1, of rat or human or rhesus, screening for **bivalent** nuclear acid ligands binding to; synthesis and identification of **bivalent** binding RNA mols. to G protein-coupled receptors)

INDEX TERM: Dopamine receptors  
ROLE: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)  
(D2, of rat or human or mouse, screening for **bivalent** nuclear acid ligands binding to; synthesis and identification of **bivalent** binding RNA mols. to G protein-coupled receptors)

INDEX TERM: Dopamine receptors  
ROLE: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)  
(D3, of rat or human, screening for **bivalent** nuclear acid ligands binding to; synthesis and identification of **bivalent** binding RNA mols. to G protein-coupled receptors)

INDEX TERM: Dopamine receptors  
ROLE: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)  
(D4, of human, screening for **bivalent** nuclear acid ligands binding to; synthesis and identification of **bivalent** binding RNA mols. to G protein-coupled receptors)

INDEX TERM: Dopamine receptors  
ROLE: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)  
(D5, of rat or human, screening for **bivalent** nuclear acid ligands binding to; synthesis and identification of **bivalent** binding RNA mols. to G protein-coupled receptors)

INDEX TERM: Endothelin receptors  
ROLE: BUU (Biological use, unclassified); BIOL (Biological

study); USES (Uses)  
(ETB, of human, screening for **bivalent** nuclear acid ligands binding to peptides of; synthesis and identification of **bivalent** binding RNA mols. to G protein-coupled receptors)

INDEX TERM: 5-HT receptors  
ROLE: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)  
(GP2-7 or 5A or 5A(S12) or 5B, of mouse/human, screening for **bivalent** nuclear acid ligands binding to peptides of; synthesis and identification of **bivalent** binding RNA mols. to G protein-coupled receptors)

INDEX TERM: Histamine receptors  
ROLE: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)  
(H1, of bovine, screening for **bivalent** nuclear acid ligands binding to; synthesis and identification of **bivalent** binding RNA mols. to G protein-coupled receptors)

INDEX TERM: Histamine receptors  
ROLE: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)  
(H2, of rat or canine or human, screening for **bivalent** nuclear acid ligands binding to; synthesis and identification of **bivalent** binding RNA mols. to G protein-coupled receptors)

INDEX TERM: Muscarinic receptors  
ROLE: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)  
(M1, of mouse or human, screening for **bivalent** nuclear acid ligands binding to; synthesis and identification of **bivalent** binding RNA mols. to G protein-coupled receptors)

INDEX TERM: Muscarinic receptors  
ROLE: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)  
(M2, of human, screening for **bivalent** nuclear acid ligands binding to; synthesis and identification of **bivalent** binding RNA mols. to G protein-coupled receptors)

INDEX TERM: Muscarinic receptors  
ROLE: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)  
(M3, of human, screening for **bivalent** nuclear acid ligands binding to; synthesis and identification of **bivalent** binding RNA mols. to G protein-coupled receptors)

INDEX TERM: Muscarinic receptors  
ROLE: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)  
(M4, of human or chicken, screening for **bivalent** nuclear acid ligands binding to; synthesis and identification of **bivalent** binding RNA mols. to G protein-coupled receptors)

INDEX TERM: Muscarinic receptors  
ROLE: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)  
(M5, of human/rat, screening for **bivalent** nuclear acid ligands binding to; synthesis and identification of **bivalent** binding RNA mols. to G protein-coupled receptors)

INDEX TERM: Tachykinin receptors  
ROLE: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)  
(NK1, of human/mouse/rat, screening for **bivalent** nuclear acid ligands binding to peptides of; synthesis and identification of **bivalent** binding RNA mols. to G protein-coupled receptors)

INDEX TERM: Oligonucleotides  
ROLE: BAC (Biological activity or effector, except adverse); BPN (Biosynthetic preparation); BSU (Biological study, unclassified); PUR (Purification or recovery); BIOL (Biological study); PREP (Preparation)  
(RNA **aptamers**, binding to G protein coupled-receptor epitopes; synthesis and identification of **bivalent** binding RNA mols. to G protein-coupled receptors)

INDEX TERM: Genetic methods  
(SELEX; synthesis and identification of **bivalent** binding RNA mols. to G protein-coupled receptors)

INDEX TERM: Somatostatin receptors  
ROLE: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)  
(SSTR1, of rat/human, screening for **bivalent** nuclear acid ligands binding to peptides of; synthesis and identification of **bivalent** binding RNA mols. to G protein-coupled receptors)

INDEX TERM: Somatostatin receptors  
ROLE: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)  
(SSTR2, of mouse, screening for **bivalent** nuclear acid ligands binding to peptides of; synthesis and identification of **bivalent** binding RNA mols. to G protein-coupled receptors)

INDEX TERM: Somatostatin receptors  
ROLE: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)  
(SSTR3, of rat/human/mouse, screening for **bivalent** nuclear acid ligands binding to peptides of; synthesis and identification of **bivalent** binding RNA mols. to G protein-coupled receptors)

INDEX TERM: Somatostatin receptors  
ROLE: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)  
(SSTR4, of human/mouse, screening for **bivalent** nuclear acid ligands binding to peptides of; synthesis and identification of **bivalent** binding RNA mols. to G protein-coupled receptors)

INDEX TERM: Somatostatin receptors  
ROLE: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)  
(SSTR5, of human/mouse, screening for **bivalent** nuclear acid ligands binding to peptides of; synthesis and identification of **bivalent** binding RNA mols. to G protein-coupled receptors)

INDEX TERM: Polysiloxanes, biological studies  
ROLE: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)  
(amino, **aptamers** linked by; synthesis and identification of **bivalent** binding RNA mols. to G protein-coupled receptors)

INDEX TERM: Angiotensin receptors  
ROLE: BUU (Biological use, unclassified); BIOL (Biological

study); USES (Uses)  
(angiotensin II, of human/rat/mouse, screening for  
**bivalent** nuclear acid ligands binding to peptides  
of; synthesis and identification of **bivalent**  
binding RNA mols. to G protein-coupled receptors)

INDEX TERM: Liposomes  
(aptamers linked by; synthesis and  
identification of **bivalent** binding RNA mols. to  
G protein-coupled receptors)

INDEX TERM: Hydrocarbons, biological studies

Monosaccharides

Oligosaccharides, biological studies

Peptides, biological studies

Polynucleotides

Polyoxyalkylenes, biological studies

Proteins, general, biological studies

ROLE: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)  
(aptamers linked by; synthesis and  
identification of **bivalent** binding RNA mols. to  
G protein-coupled receptors)

INDEX TERM: Cholecystokinin receptors  
ROLE: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)  
(cholecystokinin A, of human/rat, screening for  
**bivalent** nuclear acid ligands binding to peptides  
of; synthesis and identification of **bivalent**  
binding RNA mols. to G protein-coupled receptors)

INDEX TERM: Cholecystokinin receptors  
ROLE: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)  
(cholecystokinin B, of canine or human, screening for  
**bivalent** nuclear acid ligands binding to peptides  
of; synthesis and identification of **bivalent**  
binding RNA mols. to G protein-coupled receptors)

INDEX TERM: Polysiloxanes, biological studies  
ROLE: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)  
(hydroxy, aptamers linked by; synthesis and  
identification of **bivalent** binding RNA mols. to  
G protein-coupled receptors)

INDEX TERM: DNA  
ROLE: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)  
(linker, for generation of **bivalent** RNA ligands  
to G protein-coupled receptors epitopes; synthesis and  
identification of **bivalent** binding RNA mols. to  
G protein-coupled receptors)

INDEX TERM: Epitopes  
(of G protein-coupled receptors; synthesis and  
identification of **bivalent** binding RNA mols. to  
G protein-coupled receptors)

INDEX TERM: Thyrotropin receptors  
ROLE: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)  
(of canine/rat or human, screening for **bivalent**  
nuclear acid ligands binding to peptides of; synthesis  
and identification of **bivalent** binding RNA  
mols. to G protein-coupled receptors)

INDEX TERM: Gonadotropin-releasing hormone receptor

VIP receptors  
ROLE: BUU (Biological use, unclassified); BIOL (Biological

INDEX TERM: study); USES (Uses)  
(of human, screening for **bivalent** nuclear acid ligands binding to peptides of; synthesis and identification of **bivalent** binding RNA mols. to G protein-coupled receptors)  
Gonadotropin receptors  
ROLE: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)  
(of human/rat/mouse, screening for **bivalent** nuclear acid ligands binding to peptides of; synthesis and identification of **bivalent** binding RNA mols. to G protein-coupled receptors)  
INDEX TERM: Calcitonin receptors  
ROLE: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)  
(of human/rat/pig, screening for **bivalent** nuclear acid ligands binding to peptides of; synthesis and identification of **bivalent** binding RNA mols. to G protein-coupled receptors)  
INDEX TERM: Corticotropin releasing factor receptors  
Glucagon receptors  
Growth hormone-releasing hormone receptors  
Neuropeptide Y receptors  
ROLE: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)  
(of rat, screening for **bivalent** nuclear acid ligands binding to peptides of; synthesis and identification of **bivalent** binding RNA mols. to G protein-coupled receptors)  
INDEX TERM: Muscarinic receptors  
ROLE: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)  
(of swine or Drosophila, screening for **bivalent** nuclear acid ligands binding to; synthesis and identification of **bivalent** binding RNA mols. to G protein-coupled receptors)  
INDEX TERM: Affinity chromatography  
(screening for **bivalent** ligand to G protein-coupled receptors epitopes; synthesis and identification of **bivalent** binding RNA mols. to G protein-coupled receptors)  
INDEX TERM: G protein-coupled receptors  
ROLE: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)  
(synthesis and identification of **bivalent** binding RNA mols. to G protein-coupled receptors)  
INDEX TERM: Polysiloxanes, biological studies  
ROLE: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)  
(thio or carboxy-functionalized, **aptamers** linked by; synthesis and identification of **bivalent** binding RNA mols. to G protein-coupled receptors)  
INDEX TERM: PCR (polymerase chain reaction)  
(to link G protein coupled receptor epitope ECL1- or ECL2-binding RNA mols.; synthesis and identification of **bivalent** binding RNA mols. to G protein-coupled receptors)  
INDEX TERM: Opioid receptors  
ROLE: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)  
( $\kappa$ -opioid, of human/rat/mouse, screening for

INDEX TERM: Adrenoceptors  
ROLE: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)  
( $\alpha$ 1, of hamster or bovine, screening for  
**bivalent** nuclear acid ligands binding to;  
synthesis and identification of **bivalent**  
binding RNA mols. to G protein-coupled receptors)

INDEX TERM: Adrenoceptors  
ROLE: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)  
( $\alpha$ 1D, of rat, screening for **bivalent**  
nuclear acid ligands binding to; synthesis and  
identification of **bivalent** binding RNA mols. to  
G protein-coupled receptors)

INDEX TERM: Adrenoceptors  
ROLE: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)  
( $\alpha$ 2, D, of human or rat, screening for  
**bivalent** nuclear acid ligands binding to;  
synthesis and identification of **bivalent**  
binding RNA mols. to G protein-coupled receptors)

INDEX TERM: Adrenoceptors  
ROLE: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)  
( $\alpha$ 2, of human or mouse or fish, screening for  
**bivalent** nuclear acid ligands binding to;  
synthesis and identification of **bivalent**  
binding RNA mols. to G protein-coupled receptors)

INDEX TERM: Adrenoceptors  
ROLE: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)  
( $\alpha$ 2A, of human or porcine or rat, screening for  
**bivalent** nuclear acid ligands binding to;  
synthesis and identification of **bivalent**  
binding RNA mols. to G protein-coupled receptors)

INDEX TERM: Adrenoceptors  
ROLE: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)  
( $\alpha$ 2B, of human or rat, screening for  
**bivalent** nuclear acid ligands binding to;  
synthesis and identification of **bivalent**  
binding RNA mols. to G protein-coupled receptors)

INDEX TERM: Adrenoceptors  
ROLE: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)  
( $\alpha$ 2C, of mouse or rat, screening for  
**bivalent** nuclear acid ligands binding to;  
synthesis and identification of **bivalent**  
binding RNA mols. to G protein-coupled receptors)

INDEX TERM: Adrenoceptors  
ROLE: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)  
( $\beta$ 1, of rat or human or mouse, screening for  
**bivalent** nuclear acid ligands binding to;  
synthesis and identification of **bivalent**  
binding RNA mols. to G protein-coupled receptors)

INDEX TERM: Adrenoceptors  
ROLE: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)

INDEX TERM: Adrenoceptors  
ROLE: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)  
( $\beta$ 2, of rat or human or mouse, screening for **bivalent** nuclear acid ligands binding to; synthesis and identification of **bivalent** binding RNA mols. to G protein-coupled receptors)

INDEX TERM: Opioid receptors  
ROLE: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)  
( $\delta$ -opioid, of human/mouse, screening for **bivalent** nuclear acid ligands binding to; synthesis and identification of **bivalent** binding RNA mols. to G protein-coupled receptors)

INDEX TERM: Opioid receptors  
ROLE: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)  
( $\mu$ -opioid, of human/rat, screening for **bivalent** nuclear acid ligands binding to; synthesis and identification of **bivalent** binding RNA mols. to G protein-coupled receptors)

INDEX TERM: 79-10-7D, 2-Propenoic acid, polymers 9002-89-5  
9004-53-9, Dextrin 12619-70-4, Cyclodextrin 25322-68-3  
25322-69-4  
ROLE: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)  
(aptamers linked by; synthesis and identification of **bivalent** binding RNA mols. to G protein-coupled receptors)

INDEX TERM: 268720-50-9P, RNA (synthetic)  
ROLE: BAC (Biological activity or effector, except adverse); BPN (Biosynthetic preparation); BSU (Biological study, unclassified); PUR (Purification or recovery); BIOL (Biological study); PREP (Preparation)  
(as ligands to G protein coupled-receptor; synthesis and identification of **bivalent** binding RNA mols. to G protein-coupled receptors)

INDEX TERM: 255916-21-3 255916-22-4  
ROLE: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)  
(neurokinin receptor 1 NK1R epitope; synthesis and identification of **bivalent** binding RNA mols. to G protein-coupled receptors)

REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD.

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ACCESSION NUMBER: 1999:5968 CAPLUS

DOCUMENT NUMBER: 130:222045

ENTRY DATE: Entered STN: 06 Jan 1999

TITLE: Anti-L-selectin oligonucleotide ligands recognize CD62L-positive leukocytes: binding affinity and specificity of univalent and **bivalent** ligands

AUTHOR(S): Ringquist, Steven; Parma, David  
CORPORATE SOURCE: NeXstar Pharmaceuticals, Inc., Boulder, CO, 80301, USA  
SOURCE: Cytometry (1998), 33(4), 394-405  
CODEN: CYTODQ; ISSN: 0196-4763  
PUBLISHER: Wiley-Liss, Inc.  
DOCUMENT TYPE: Journal  
LANGUAGE: English  
CLASSIFICATION: 15-10 (Immunochemistry)

**ABSTRACT:**  
Oligonucleotide **aptamers** generated against purified LS-Rg, a human L-selectin/IgG fusion protein, bound human CD62L-pos. leukocytes. FACS anal. of lymphocytes or neutrophils stained with fluorescently labeled **aptamers** indicated specificity and sensitivity for cellular L-selectin similar to that observed with anti-L-selectin antibody. Univalent **aptamers** were compared to **bivalent aptamers** as well as to the anti-adhesion, anti-L-selectin antibody DREG56. Equilibrium and kinetic binding expts. were performed to examine the affinity and kinetic binding parameters of L-selectin **aptamers** to evaluate their binding to CD62L-pos. leukocytes and to test their potential as L-selectin antagonists. Binding expts. indicated that **bivalent aptamers** approached the affinity and the dissociation rate of **bivalent antibody**, and preferentially recognized cellular compared to soluble L-selectin, a potentially useful distinction *in vivo*. Anti-L-selectin **aptamers** also inhibited L-selectin dependent self-adhesion of neutrophils, suggesting that *in vitro* univalent and **bivalent aptamers** provided anti-adhesion activity similar to that observed with blocking antibody and indicated a direct blocking mechanism of action during inhibition of L-selectin-dependent trafficking of lymphocytes *in vivo*.

SUPPL. TERM: L selectin oligonucleotide ligand leukocyte  
INDEX TERM: Selectins  
ROLE: BSU (Biological study, unclassified); BIOL (Biological study)  
(L-; anti-L-selectin oligonucleotide ligands recognize CD62L-pos. leukocytes)  
INDEX TERM: Leukocyte  
(adhesion; anti-L-selectin oligonucleotide ligands recognize CD62L-pos. leukocytes)  
INDEX TERM: Leukocyte  
Neutrophil  
(anti-L-selectin oligonucleotide ligands recognize CD62L-pos. leukocytes)  
INDEX TERM: Oligonucleotides  
ROLE: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)  
(anti-L-selectin oligonucleotide ligands recognize CD62L-pos. leukocytes)  
INDEX TERM: Cell adhesion  
(leukocyte; anti-L-selectin oligonucleotide ligands recognize CD62L-pos. leukocytes)  
REFERENCE COUNT: 81 THERE ARE 81 CITED REFERENCES AVAILABLE FOR THIS RECORD.  
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L11 ANSWER 17 OF 17 CAPLUS COPYRIGHT 2005 ACS on STN  
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 INVENTOR(S): Gabriel, Dean W.  
 PATENT ASSIGNEE(S): University of Florida, USA  
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RW: GH, KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
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ABSTRACT:

The subject invention pertains to materials and methods that provide plants with resistance to plant pathogens and pests. Antibodies and **aptamers**

that immunoreact or bind and inhibit the action of protein expression products from avirulence and/or pathogenicity genes, including, but not limited to, the *Xanthomonas* *avr*/*pth* family of such genes, are described. The antibodies of the subject invention function by blocking the action of the primary protein products of *avr*/*pth* genes by intercepting and denaturing them prior to their translocation to the plant nucleus. The method of the subject invention concerns transforming a plant with polynucleotide mols. that encode the antibodies. Expression of the antibodies in the plant confers resistance from pathogens and pests. The subject invention also pertains to polynucleotide mols. encoding the subject antibodies, as well as plants and plant tissue transformed with the polynucleotide mols. encoding the subject antibodies.

SUPPL. TERM: avirulence protein antibody plant pathogen resistance; pathogenicity protein antibody plant pathogen resistance; *avr* gene antibody plant pathogen resistance; *pth* gene antibody plant pathogen resistance; genetic engineering plant pathogen resistance antibody; *Xanthomonas* antibody plant pathogen resistance transformation

INDEX TERM: Proteins, specific or class  
ROLE: ADV (Adverse effect, including toxicity); AGR (Agricultural use); BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process); USES (Uses)  
(*Avr4*; antibodies against avirulence/pathogenicity proteins of plant pathogens and use to genetically engineer pathogen resistant plants)

INDEX TERM: Proteins, specific or class  
ROLE: ADV (Adverse effect, including toxicity); AGR (Agricultural use); BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process); USES (Uses)  
(*AvrB101*; antibodies against avirulence/pathogenicity proteins of plant pathogens and use to genetically engineer pathogen resistant plants)

INDEX TERM: Proteins, specific or class  
ROLE: ADV (Adverse effect, including toxicity); AGR (Agricultural use); BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process); USES (Uses)  
(*AvrB102*; antibodies against avirulence/pathogenicity proteins of plant pathogens and use to genetically engineer pathogen resistant plants)

INDEX TERM: Proteins, specific or class  
ROLE: ADV (Adverse effect, including toxicity); AGR (Agricultural use); BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process); USES (Uses)  
(*AvrB4*; antibodies against avirulence/pathogenicity proteins of plant pathogens and use to genetically engineer pathogen resistant plants)

INDEX TERM: Proteins, specific or class  
ROLE: ADV (Adverse effect, including toxicity); AGR (Agricultural use); BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process); USES (Uses)  
(*AvrB6*; antibodies against avirulence/pathogenicity proteins of plant pathogens and use to genetically engineer pathogen resistant plants)

INDEX TERM: Proteins, specific or class  
ROLE: ADV (Adverse effect, including toxicity); AGR (Agricultural use); BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study);

INDEX TERM: PROC (Process); USES (Uses)  
(AvrB7; antibodies against avirulence/pathogenicity  
proteins of plant pathogens and use to genetically  
engineer pathogen resistant plants)

INDEX TERM: Proteins, specific or class  
ROLE: ADV (Adverse effect, including toxicity); AGR  
(Agricultural use); BPR (Biological process); BSU  
(Biological study, unclassified); BIOL (Biological study);  
PROC (Process); USES (Uses)  
(AvrBs3; antibodies against avirulence/pathogenicity  
proteins of plant pathogens and use to genetically  
engineer pathogen resistant plants)

INDEX TERM: Proteins, specific or class  
ROLE: ADV (Adverse effect, including toxicity); AGR  
(Agricultural use); BPR (Biological process); BSU  
(Biological study, unclassified); BIOL (Biological study);  
PROC (Process); USES (Uses)  
(AvrXa10; antibodies against avirulence/pathogenicity  
proteins of plant pathogens and use to genetically  
engineer pathogen resistant plants)

INDEX TERM: Proteins, specific or class  
ROLE: ADV (Adverse effect, including toxicity); AGR  
(Agricultural use); BPR (Biological process); BSU  
(Biological study, unclassified); BIOL (Biological study);  
PROC (Process); USES (Uses)  
(AvrXa7; antibodies against avirulence/pathogenicity  
proteins of plant pathogens and use to genetically  
engineer pathogen resistant plants)

INDEX TERM: Proteins, specific or class  
ROLE: ADV (Adverse effect, including toxicity); AGR  
(Agricultural use); BPR (Biological process); BSU  
(Biological study, unclassified); BIOL (Biological study);  
PROC (Process); USES (Uses)  
(PthA; antibodies against avirulence/pathogenicity  
proteins of plant pathogens and use to genetically  
engineer pathogen resistant plants)

INDEX TERM: Proteins, specific or class  
ROLE: ADV (Adverse effect, including toxicity); AGR  
(Agricultural use); BPR (Biological process); BSU  
(Biological study, unclassified); BIOL (Biological study);  
PROC (Process); USES (Uses)  
(PthB; antibodies against avirulence/pathogenicity  
proteins of plant pathogens and use to genetically  
engineer pathogen resistant plants)

INDEX TERM: Proteins, specific or class  
ROLE: ADV (Adverse effect, including toxicity); AGR  
(Agricultural use); BPR (Biological process); BSU  
(Biological study, unclassified); BIOL (Biological study);  
PROC (Process); USES (Uses)  
(PthC; antibodies against avirulence/pathogenicity  
proteins of plant pathogens and use to genetically  
engineer pathogen resistant plants)

INDEX TERM: Proteins, specific or class  
ROLE: ADV (Adverse effect, including toxicity); AGR  
(Agricultural use); BPR (Biological process); BSU  
(Biological study, unclassified); BIOL (Biological study);  
PROC (Process); USES (Uses)  
(PthN; antibodies against avirulence/pathogenicity  
proteins of plant pathogens and use to genetically  
engineer pathogen resistant plants)

INDEX TERM: Proteins, specific or class  
ROLE: ADV (Adverse effect, including toxicity); AGR

INDEX TERM: (Agricultural use); BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process); USES (Uses)  
(PthP; antibodies against avirulence/pathogenicity proteins of plant pathogens and use to genetically engineer pathogen resistant plants)

INDEX TERM: Proteins, specific or class  
ROLE: ADV (Adverse effect, including toxicity); AGR (Agricultural use); BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process); USES (Uses)  
(PthPC; antibodies against avirulence/pathogenicity proteins of plant pathogens and use to genetically engineer pathogen resistant plants)

INDEX TERM: Disease resistance, plant  
Genetic engineering  
Plant pathogen  
Transformation, genetic  
Xanthomonas  
(antibodies against avirulence/pathogenicity proteins of plant pathogens and use to genetically engineer pathogen resistant plants)

INDEX TERM: Antibodies  
Immunoglobulins  
ROLE: AGR (Agricultural use); BAC (Biological activity or effector, except adverse); BPN (Biosynthetic preparation); BSU (Biological study, unclassified); BIOL (Biological study); PREP (Preparation); USES (Uses)  
(antibodies against avirulence/pathogenicity proteins of plant pathogens and use to genetically engineer pathogen resistant plants)

INDEX TERM: Gene, microbial  
ROLE: BSU (Biological study, unclassified); BIOL (Biological study)  
(avr; antibodies against avirulence/pathogenicity proteins of plant pathogens and use to genetically engineer pathogen resistant plants)

INDEX TERM: Antibodies  
ROLE: AGR (Agricultural use); BAC (Biological activity or effector, except adverse); BPN (Biosynthetic preparation); BSU (Biological study, unclassified); BIOL (Biological study); PREP (Preparation); USES (Uses)  
(bivalent; antibodies against avirulence/pathogenicity proteins of plant pathogens and use to genetically engineer pathogen resistant plants)

INDEX TERM: Proteins, specific or class  
ROLE: ADV (Adverse effect, including toxicity); AGR (Agricultural use); BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process); USES (Uses)  
(gene avr, avirulence; antibodies against avirulence/pathogenicity proteins of plant pathogens and use to genetically engineer pathogen resistant plants)

INDEX TERM: Proteins, specific or class  
ROLE: ADV (Adverse effect, including toxicity); AGR (Agricultural use); BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process); USES (Uses)  
(gene pth, pathogenicity; antibodies against avirulence/pathogenicity proteins of plant pathogens and use to genetically engineer pathogen resistant plants)

INDEX TERM: Proteins, specific or class

INDEX TERM: **ROLE: ADV (Adverse effect, including toxicity); AGR (Agricultural use); BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process); USES (Uses)**  
**(hrpN; antibodies against avirulence/pathogenicity proteins of plant pathogens and use to genetically engineer pathogen resistant plants)**

INDEX TERM: **Proteins, specific or class**  
ROLE: ADV (Adverse effect, including toxicity); AGR (Agricultural use); BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process); USES (Uses)  
**(hrpZ; antibodies against avirulence/pathogenicity proteins of plant pathogens and use to genetically engineer pathogen resistant plants)**

INDEX TERM: **Antibodies**  
ROLE: AGR (Agricultural use); BAC (Biological activity or effector, except adverse); BPN (Biosynthetic preparation); BSU (Biological study, unclassified); BIOL (Biological study); PREP (Preparation); USES (Uses)  
**(monovalent; antibodies against avirulence/pathogenicity proteins of plant pathogens and use to genetically engineer pathogen resistant plants)**

INDEX TERM: **Antibodies**  
ROLE: AGR (Agricultural use); BAC (Biological activity or effector, except adverse); BPN (Biosynthetic preparation); BSU (Biological study, unclassified); BIOL (Biological study); PREP (Preparation); USES (Uses)  
**(nuclear localization signal-comprising; antibodies against avirulence/pathogenicity proteins of plant pathogens and use to genetically engineer pathogen resistant plants)**

INDEX TERM: **Denaturation**  
**(protein, by antibody; antibodies against avirulence/pathogenicity proteins of plant pathogens and use to genetically engineer pathogen resistant plants)**

INDEX TERM: **Gene, microbial**  
ROLE: BSU (Biological study, unclassified); BIOL (Biological study)  
**(pth; antibodies against avirulence/pathogenicity proteins of plant pathogens and use to genetically engineer pathogen resistant plants)**

INDEX TERM: **Plant cell**  
**(transformed; antibodies against avirulence/pathogenicity proteins of plant pathogens and use to genetically engineer pathogen resistant plants)**

INDEX TERM: **Dicotyledon (Magnoliopsida)**

INDEX TERM: **Monocotyledon (Liliopsida)**

INDEX TERM: **Plant (Embryophyta)**

INDEX TERM: **Plant tissue**

INDEX TERM: **Protoplast and Spheroplast**

INDEX TERM: **Seed**

INDEX TERM: **Seedling**  
**(transgenic; antibodies against avirulence/pathogenicity proteins of plant pathogens and use to genetically engineer pathogen resistant plants)**

INDEX TERM: **Cell nucleus**  
**(translocation of protein to; antibodies against avirulence/pathogenicity proteins of plant pathogens and use to genetically engineer pathogen resistant plants)**

INDEX TERM: **Recombination, genetic**  
**(translocation, of protein, to nucleus; antibodies**

against avirulence/pathogenicity proteins of plant pathogens and use to genetically engineer pathogen resistant plants)

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